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The American Heart Journal

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Original Communications

GALLOP RHYTHM AND THE PHYSIOLOGICAL THIRD HEART SOUND

I. CHARACTERISTICS OF THE SOUNDS, CLASSIFICATION, COMPARATIVE INCIDENCE OF THE VARIOUS TYPES AND DIFFERENTIAL DIAGNOSIS*

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THERE is considerable disagreement in the literature concerning the characteristics and significance of gallop rhythm and its relation to the physiological third heart sound. The differences of opinion are clearly stated in Holt's[1] excellent review of the subject. During the past four years we have been collecting clinical material and applying various laboratory methods in an effort to obtain data bearing on these problems.

One of the difficulties encountered early in the work was that of fitting certain cases into proper categories. There is no doubt as to the usefulness of Potain's[2] classification based on time relations, in so far as it applies to protodiastolic and presystolic gallop. The relationships of the type of gallop which he called mesodiastolic, however, have not been clearly determined. Mesodiastolic gallop, according to Potain, is either presystolic or protodiastolic gallop which happens to occupy a position in mid-diastole because of tachycardia. This view was based on auscultatory studies and the position of diastolic filling waves in apex cardiograms, methods which must be recognized as inadequate. Thus the question as to whether or not mesodiastolic gallop deserves recognition as a distinct entity, has up to the present time remained unanswered.

From the above considerations it seemed that the classification of gallop rhythm was not completely satisfactory and that the subject required further investigation. We have therefore attempted to clarify the situation, and in this report offer what we believe to be a theoretically sound

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and practical classification including both gallop rhythm and physiological third heart sounds.*

MATERIAL AND METHODS

The observations on gallop rhythm and the physiological third heart sound constitute part of a more comprehensive study including the opening snap of mitral stenosis,[3] reduplication of first and second heart sounds and other sounds (exclusive of murmurs) heard during the cardiac cycle. The material was obtained from all available sources, chiefly hospital ward and outpatient departments. Private patients and University students referred to the Section for examination were also utilized. Most of the observations on which this report is based were made in 70 cases, of which 60 were classified as having gallop rhythm, and 10, physiological third heart sounds. For inclusion in the group, it was required not only that the gallop or third sound be heard on auscultation, but also that it be clearly recorded by sound registration apparatus. All patients were subjected to fairly complete physical examination, and nearly all those with gallop rhythm were under observation for periods varying from several weeks to four years.

In all cases electrocardiograms were recorded simultaneously with the sound registration. Especial care was taken to avoid parallax, so that the time relations and positions in the heart cycle of the various sound waves could be determined. The sound registration methods used have been mentioned previously.[3]

THE DIFFERENTIATION BETWEEN GALLOP AND THE PHYSIOLOGICAL THIRD HEART SOUNDS

Thayer[4] and more recently Gubergritz[5] have emphasized the similarity of physiological third heart sounds and gallop sounds. Gubergritz believes, however, that there are certain differences in quality and intensity of the sounds. We have observed no essential differences in quality, location, time relations, or the influence of posture or various maneuvers to alter the sounds. The only criterion available for differentiation, aside from the fact that physiological third heart sounds become increasingly rare with advancing age, is the status of cardiac function. When the cardiac function is obviously altered from the normal, the sounds are arbitrarily classed as gallop sounds. If no abnormality is detected, the sounds are regarded as physiological third heart sounds.

It would be more satisfactory if other criteria besides the status of cardiac function were available in youthful patients for deciding whether a third sound should be designated as a physiological third heart sound or

*The so-called systolic gallop rhythm is not considered in this paper. These systolic sounds must have a fundamentally different mechanism of production from the gallop sounds which occur during diastole. They are rarely heard, have apparently little clinical importance, and in order to avoid confusion should be given a name which does not include the term "gallop."

as part of gallop rhythm. The differentiation has considerable practical utility. The rather loud third sounds sometimes heard during hyperthyroidism, anemia, the active stages of rheumatic fever and occasionally in other infections, are clearly associated with these pathological states. They usually disappear, or at least become much less distinct, upon the subsidence of these conditions. Thus, they are a manifestation of disease and according to our present nomenclature should be called gallop rhythm.*

Physiological third heart sounds can be elicited in a considerable percentage of children and young adults provided the methods devised by Thayer[4] are employed. If already present they can sometimes be greatly intensified by these methods. Occasionally, however, instead of becoming louder the sounds vanish in left lateral decubitus, which is ordinarily the position most conducive to their appearance. The group of 10 cases included in the present study was specially selected for sound registration since all had third heart sounds easily heard in either dorsal or left lateral decubitus.

CHARACTERISTICS OF THE SOUND

a. Quality and Loudness.—Third sounds (both gallop and physiological third sounds) are almost invariably dull and low-pitched. The phenomenon has frequently been described as a "thud" or "shock" which can sometimes be more distinctly palpated than heard.† The low vibration frequency of the main oscillations in sound tracings of physiological third sounds has been pointed out by Bridgeman.[6] Gallop sounds have a similarly low vibration frequency. The sounds are characteristically short in duration. When, however, two gallop sounds occur during the same heart cycle (protodiastolic and presystolic) and the heart rate is such as to bring them close together, the resulting sound may be reduplicated, prolonged or may actually resemble a short murmur. The loudness of the sounds varies widely. As a rule, they are much less audible than the first or second sounds and may escape detection unless the examiner has them in mind. Occasionally, however, the third sound may be louder than either the first or second sound or both. (Fig. 1 and Fig. 8, lower strip.)

Respiratory variations in the loudness of gallop or physiological third sounds are present in many cases and tend to be much greater than respiratory variations in either the first or second sound. In some cases the sound may be quite loud near the end of expiration and either faint or absent when the lungs are filled. (Fig. 2.) However, independently of respiration, there is remarkable variability and inconstancy of gallop, a char-

*There is always the possibility, indeed the probability, in young patients that a physiological third heart sound might have been present before the development of a morbid state. Such a sound may be accentuated merely by the tachycardia accompanying the disease. Before designating the sound as gallop, it should be demonstrated that its presence, or at least, its accentuation was due to the disease and not merely to tachycardia.

†The sensation obtained on palpation is probably derived chiefly from the large single wave of ventricular filling.

acteristic which must impress every one who studies these sounds. This phenomenon is well exemplified in a large group of cases excluded from the present study because of the fact that, although gallop sounds had been present at the original examination, they were either no longer present or so faint that they could not be recorded satisfactorily when the patients were sent to the laboratory.

b. Location.—In the great majority of cases the gallop sound is heard best in the neighborhood of the apex impulse. (Fig. 3.) When the sound is faint, it may be sharply limited to this position. When it is loud, however, it may be heard over a considerable area. Occasionally gallop sounds are heard best over or just to the left of the lower end of the sternum.

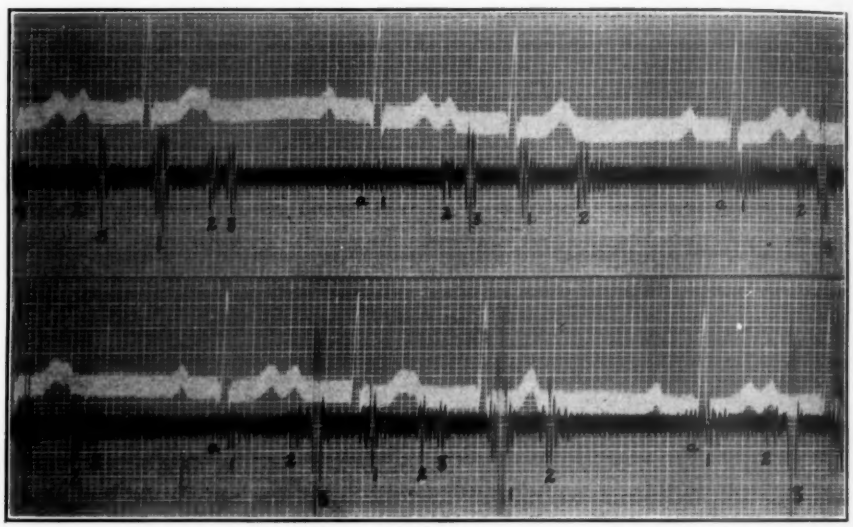

Fig. 1.—Incomplete heart-block and gallop rhythm occurring in a boy fourteen years old following an attack of streptococcic sore throat. (Continuous tracing.) Marked variation in amplitude of vibrations of gallop sounds. The small vibrations marked "a" are due to auricular activity alone. These were not audible. The protodiastolic vibrations in beats 1 and 4 of the lower tracing are little if any influenced by auricular activity. In the last beat of the upper strip, and the second and fifth beats of the lower strip, auricular contraction falls at a time favorable for the production of very loud gallop sounds which not only have an amplitude far greater than either the first or second heart sound but on auscultation were found to be much louder. The variations in intensity of the first heart sound are due to varying A-V relations.[16]

Among our cases the sound was heard best over the apical area in 53, near the lower edge of the sternum in 3; while in 2 cases it was sometimes louder at the apex, and sometimes louder near the lower edge of the sternum.

In all individuals with physiological third heart sounds whom we have studied, the third sound was heard best in the region of the apex impulse. As in gallop, when the sound is loud, it may be well heard over a considerable area.

c. Time Relations.—In the cases of third heart sound studied by Bridgeman,[6] the interval between the beginning of the second and third sounds ranged from 0.13 to 0.18 second. Bridgeman noted that small presystolic

vibrations were also present in the sound records of 11 out of 16 cases. He states that these "sounds" are "generally" below the limit of human audibility. Battaerd,[7] and Michaud and Fleisch[8] have also recorded these apparently subsonic presystolic vibrations. Although these small vibrations are frequently recorded (Figs. 1, 2, middle strip, 4 top strip), much larger sonic vibrations are found with the same time relations to auricular systole. (Fig. 4, bottom strip.) In such cases, a presystolic physiological

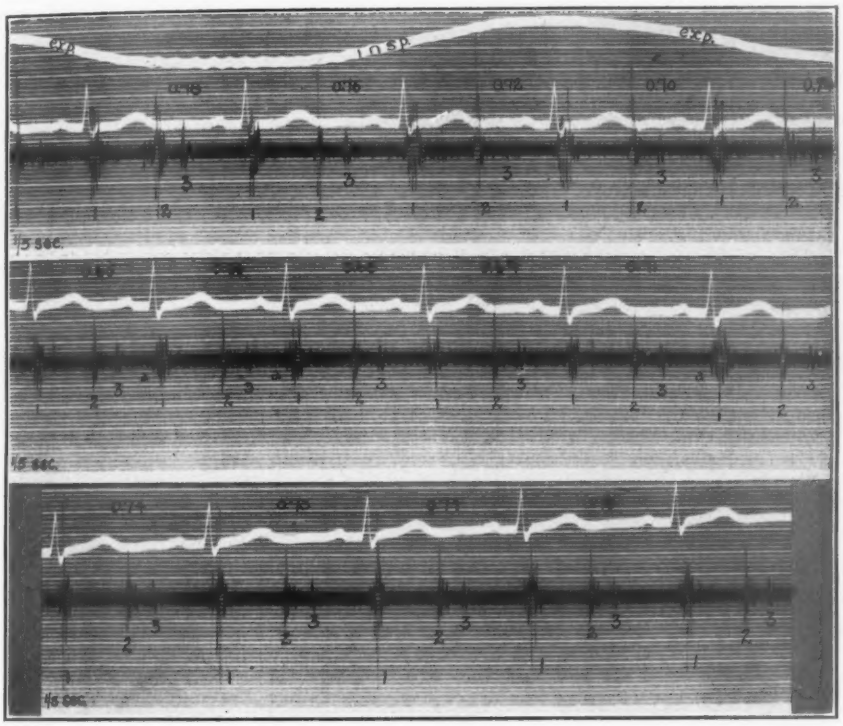

Fig. 2.—Physiological third heart sound. The top strip illustrates the effect of normal respiration. When the lungs were emptied, the third sound vibrations were decidedly larger than when the lungs were filled. On auscultation the sounds were likewise decidedly louder when the lungs were emptied. The lower two tracings were made with the breath held. The third sound vibrations are essentially the same throughout. The cycle lengths are given to show that the variations in cycle length in the top strip are not responsible for the variations in the third sound. In the second tracing subsonic presystolic vibrations (a) are recorded.

third heart sound is audible and has the same characteristics as the much more common presystolic gallop sound.

The time relations of the physiological third sound and gallop rhythm are comparatively simple. *In all of our 70 cases, without exception, the physiological third heart sounds and gallop sounds fell within one or both of two distinct time zones.* These time zones are: (1) the period of 0.10 to 0.21 second (usually 0.13 to 0.18 second) after the beginning of the second heart sound (unless the second sound is definitely split, under which circumstance the time relation is maintained with one component); and (2)

the period of 0.08 to 0.14 second after the beginning of the P-wave of the electrocardiogram.

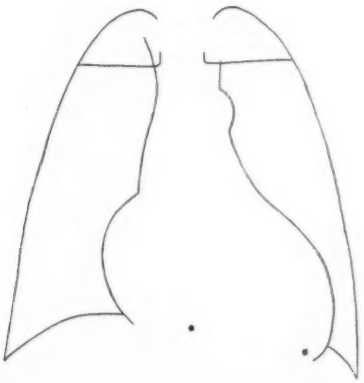

Fig. 3.—Orthodiagram made in a patient who exhibited both right and left-sided gallop rhythm. The dots represent the two positions over which the gallop sounds were best heard. The position with reference to the heart is determined by finding the point of maximum audibility of the gallop sound, fixing a lead disc on this point by adhesive tape, and marking its position on the anteroposterior silhouette by orthodiagraphy. Studies of this type made in fifteen cases of left-sided gallop all showed the gallop sound to have its maximum audibility near the apex.

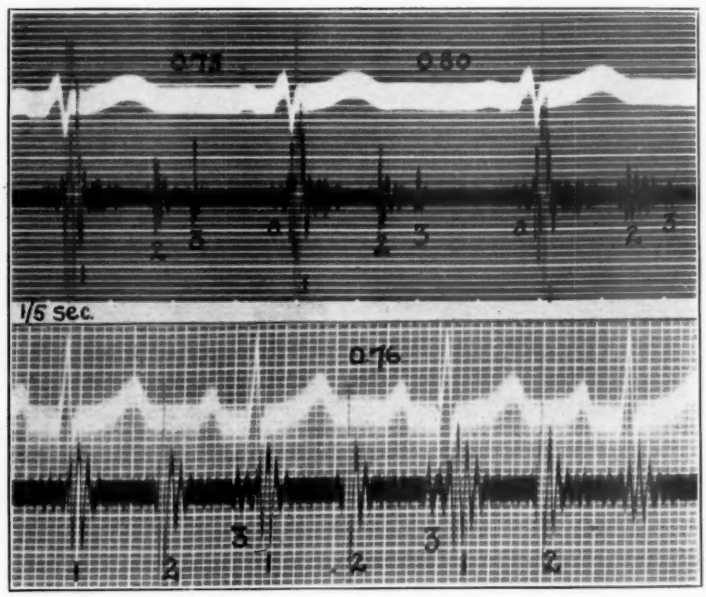

Fig. 4.—Physiological third heart sounds. The upper tracing illustrates protodiastolic third sound (3) and subsonic presystolic vibrations (a). The lower tracing shows presystolic vibrations (3) which were clearly audible as a presystolic physiological third heart sound.

Observations were made as to the effect of heart cycle length on the time relations of the sounds. In 20 cases exhibiting presystolic gallop rhythm, no correlation was observed between cardiac rate and the interval between

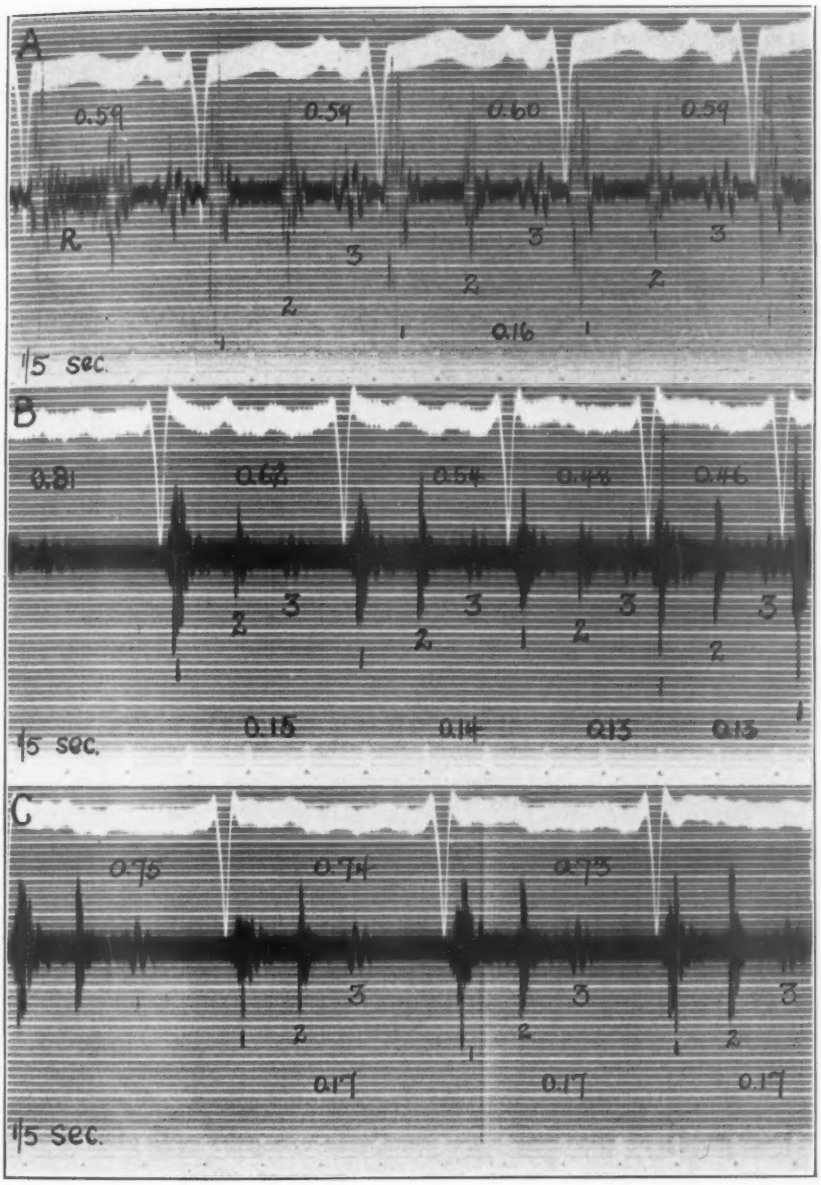

Fig. 5.—The top strip illustrates a somewhat imperfect summation gallop, the cardiac rate being approximately 100. Due to the imperfect summation, the gallop sound is prolonged. On auscultation the sound was easily heard but was not loud. The lower two strips were obtained from the same patient during auricular fibrillation. The gallop sounds were now clearly protodiastolic, shorter in duration, and faint, being heard with difficulty. There are variations in the duration of the interval between the second sound and the gallop sound (from 0.13 to 0.17 second) which shows some relation to the preceding cycle lengths.

the beginning of the P-wave and the gallop sound. In protodiastolic gallop rhythm, however, as in the case of protodiastolic physiological third heart sounds, evidence can be obtained that preceding cycle length is a factor in determining the duration of the interval between the second and protodiastolic sounds. This can be shown by studies of individual patients, comparing the intervals in sound tracings exhibiting different cardiac rates. The correlation between cardiac rate and the interval was not close for our entire group of cases; since the interval seems to be characteristically longer in some than in others. Doubtless, therefore, its duration is influenced by factors other than cardiac rate. In six cases of auricular fibrillation, exhibiting protodiastolic gallop rhythm, variations in this interval of from 0.02 to 0.04 second were noted, the shorter intervals tending to follow relatively short preceding cycle lengths, and the longer intervals relatively long preceding cycle lengths. There is, however, no accurate correlation between the duration of the interval and the preceding heart cycle. (Fig. 5.)

THE CLASSIFICATION OF GALLOP RHYTHM

What later came to be known as presystolic gallop rhythm was described by Charcelay[9] in 1838. Bouillaud[10] gave it the name "bruit de galop." It remained for Potain,[2] however, to separate gallop from other sounds, and to classify the forms as protodiastolic, mesodiastolic and presystolic.

Our sound registration studies, as well as those previously made, confirm Potain's conception of protodiastolic and presystolic forms of gallop. These sounds have the time relations which have been mentioned above. The term presystolic is not strictly accurate, since the sound which it designates is not necessarily presystolic. Thus, when the auriculoventricular conduction time is prolonged, presystolic gallop is no longer actually presystolic in time. Its position depends on the time of auricular contraction.*

We have never observed a mid-diastolic gallop sound falling outside the time zones of presystolic or protodiastolic gallop. However, when these two zones merge because of tachycardia, a gallop sound may be present and fall near the middle of the diastolic period. Such a sound may occupy a position which is approximately mesodiastolic; however, it is just as near to the preceding beat as protodiastolic gallop and to the following beat as presystolic gallop. If either protodiastolic or presystolic gallop or both be present when the rate is slow enough to keep these time zones

*On account of the sanction conferred by long usage, it does not seem advisable to attempt to substitute another name for "presystolic gallop." Duchosal[11] has used the term "auricular gallop"; although this term has certain advantages it is likewise open to objection, since it might readily lead to the misconception that the sound originates within the auricles. Duchosal has emphasized the point that it should not carry such a connotation. A fault in nomenclature analogous to that of presystolic gallop is found in the strongly entrenched term "presystolic murmur," since this murmur, like the gallop sound, is dependent on auricular contraction. The presystolic murmur, however, tends to be more prolonged than a gallop sound so that a greater delay in A-V conduction is necessary to displace it from a presystolic position.

separate, a much louder gallop sound occurs when the rate increases and they become merged. This is equally true whether the merging be due to tachycardia (in which case the gallop sounds fall about the middle of diastole) or to lengthened A-V conduction time (which may cause the sound to be protodiastolic in time). Thus the term "mesodiastolic gallop," which connotes a type separate from protodiastolic and presystolic gallop, is misleading and should be discarded. We therefore propose that

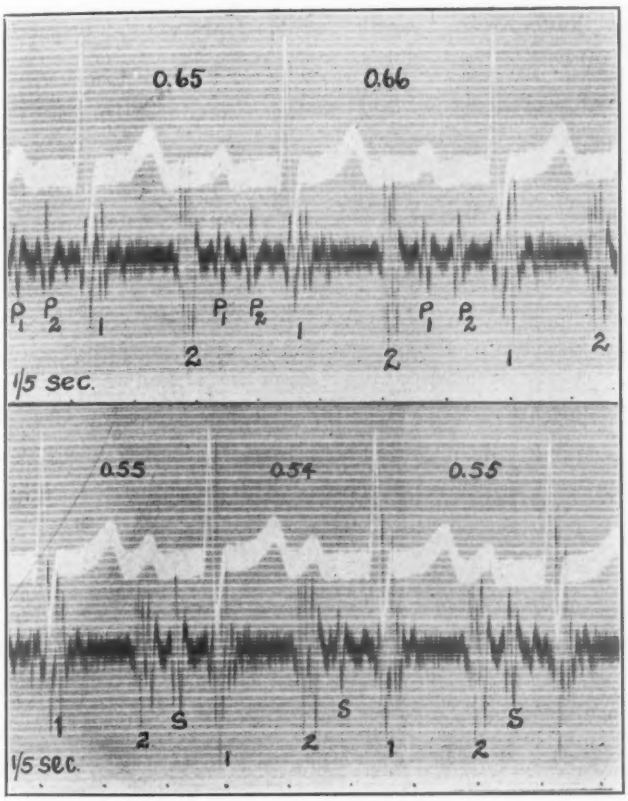

Fig. 6.—Minor grade heart-block, sinus arrhythmia and gallop rhythm. The upper tracing (taken during the period of retardation in rate) shows both protodiastolic (P_1) and presystolic (P_2) gallop. The lower tracing (taken during the period of acceleration in rate) which was part of a continuous strip with the upper shows the summation phenomenon (s). It is obvious from comparison with the second sound that the gallop sound vibrations are much larger when summation is present than when both protodiastolic and presystolic gallop are recorded as separate sound vibrations.

the type of gallop which occurs as a result of the coincidence of protodiastolic and auriculosystolic phenomena be called summation gallop.* The evidence for the occurrence of summation is based upon the effect of

*The term "summation gallop" was proposed by us in 1931 in the discussion of a classification of "extra" or additional heart sounds.[12] Summation (as used in psychology and physiology) is defined in Funk and Wagnall's dictionary as "The aggregate influence of several stimuli producing a sensible effect that no one alone would produce." It is in this sense that we apply the term rather than in accordance with its usage in physics (as summation tone).

rate changes, including sinus arrhythmia, auricular fibrillation, heart-block, ventricular and auricular extrasystoles on gallop sounds.*

1. Effect of Variations in Rate.—In two cases exhibiting both faint protodiastolic and presystolic gallop sounds when the heart rate was approximately normal, it was found that, as the heart rate was increased, there was a critical level at which the two gallop sounds merged, with the production of a single comparatively loud sound. When the heart rate again fell below the critical level, the loud gallop sound disappeared, being replaced by the two faint sounds originally present. In one of the cases

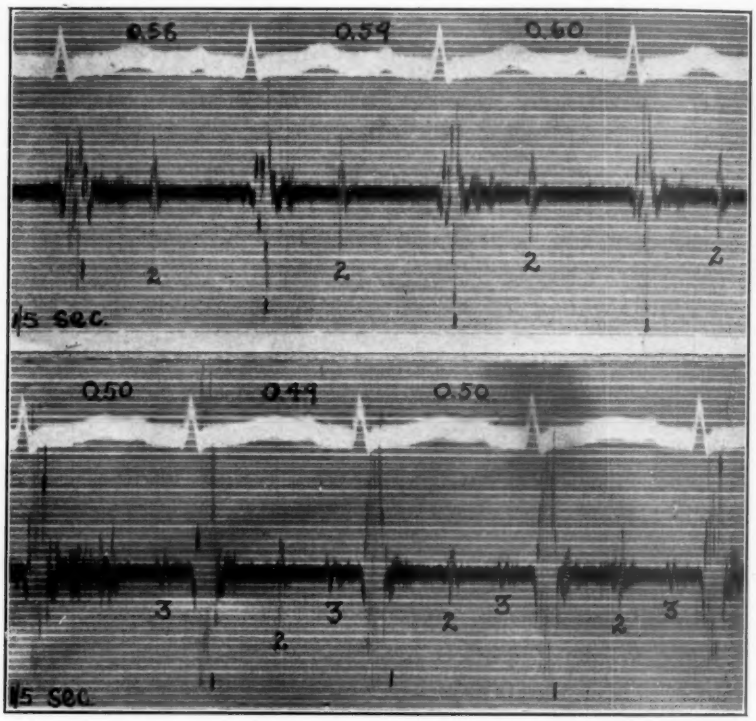

Fig. 7.—In the upper tracing the cardiac rate was 100, and no gallop sound was recorded. In the lower tracing made after elevating the rate to 120 by amyl nitrite so that auricular systole was superimposed on the protodiastolic phase of the preceding beat, a distinct gallop sound appeared.

the critical rate was sometimes attained during the phase of acceleration of sinus arrhythmia (Fig. 6).

It was repeatedly noted, both on auscultation and in sound tracings, that the critical level at which a gallop sound appears or, if already present (either presystolic or protodiastolic) suddenly becomes loud, is the rate at

*It has been shown that acceleration in the process of ventricular filling occurs in the protodiastolic period immediately after ventricular relaxation and also following auricular contraction. Most writers on gallop rhythm support the view that gallop sounds are in some way associated with waves of ventricular filling. Thus, when the two factors associated with acceleration of ventricular filling are superimposed, one might expect a single large surge of ventricular filling and therefore marked effects on gallop sounds. In a subsequent paper we shall present new evidence bearing on this point.

which auricular systole is superimposed upon the preceding protodiastolic period. (Fig. 7.) This rate in our cases was usually within the range of 100 to 130, depending on such factors as the length of the P-R interval and the duration of ventricular systole.* Doubtless also, the rapidity of isometric ventricular relaxation was a factor, but this could not be satisfactorily measured at rapid rates.† If the P-R interval was prolonged, the critical rate at which loud gallop sounds occurred tended to be lower. Thus in one case, with a P-R interval of 0.22 second, the critical level at which the loud sound appeared was between 90 and 100 beats per minute.‡

2. *Effect of Auricular Fibrillation.*—In three cases, heart sound studies were made during periods of regular rhythm and during auricular fibril-

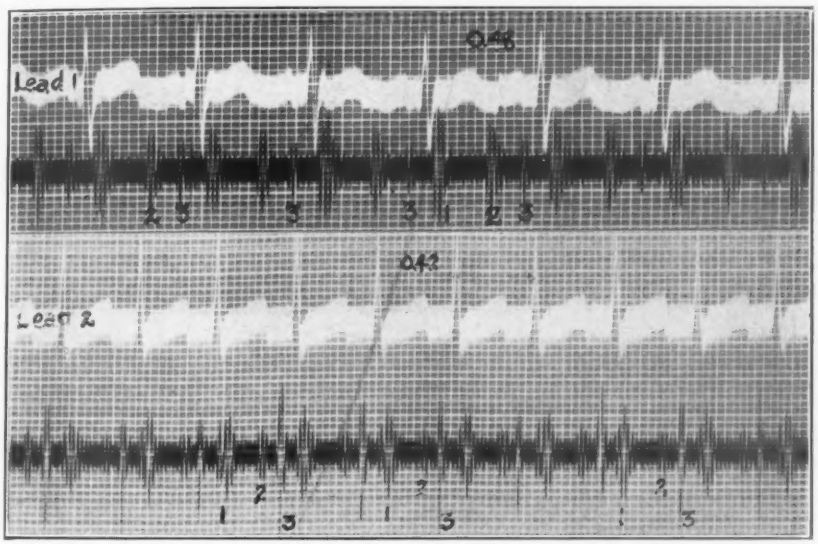

Fig. 8.—In the upper tracing the cardiac rate is 125 and summation gallop sound (3) is clearly recorded. The sound vibrations are smaller than those of either the first or the second heart sound. In the lower tracing (same patient but made on a different day) the rate is 143, and the vibrations of the gallop sound are of larger amplitude than either the first or second sound. The interval between the second and gallop sound (0.10 second) is the shortest recorded in this study. The shorter interval in the lower strip is probably due to the greater rate.

lation. In one of these cases, during normal rhythm the critical rate at which a loud gallop sound appeared was approximately 100. In the other two cases the critical rate was not determined, but the gallop sound was loud at rates of 107 and 114. In all three, however, auricular systole was

*The lowest rate at which summation occurs is not necessarily the optimum rate for the production of the loudest gallop sound. (Fig. 8.)

†The ventricular isometric relaxation phase is measured by the interval between the beginning of the second heart sound (provided the sound is not split) and the beginning of the descending limb of the V-wave in the optically recorded venous pulse in the neck. When auricular contraction falls in the protodiastolic period, the significant point in the V-wave tends to be obscured by the coincident A-wave.

‡In connection with these observations it should be emphasized that, irrespective of superimposition of auricular contraction on the preceding protodiastolic period, acceleration in rate may accentuate gallop or physiological third heart sounds, or if they are absent at slower rates, cause them to appear. In the absence of summation, however, the effect of rate changes is not so striking.

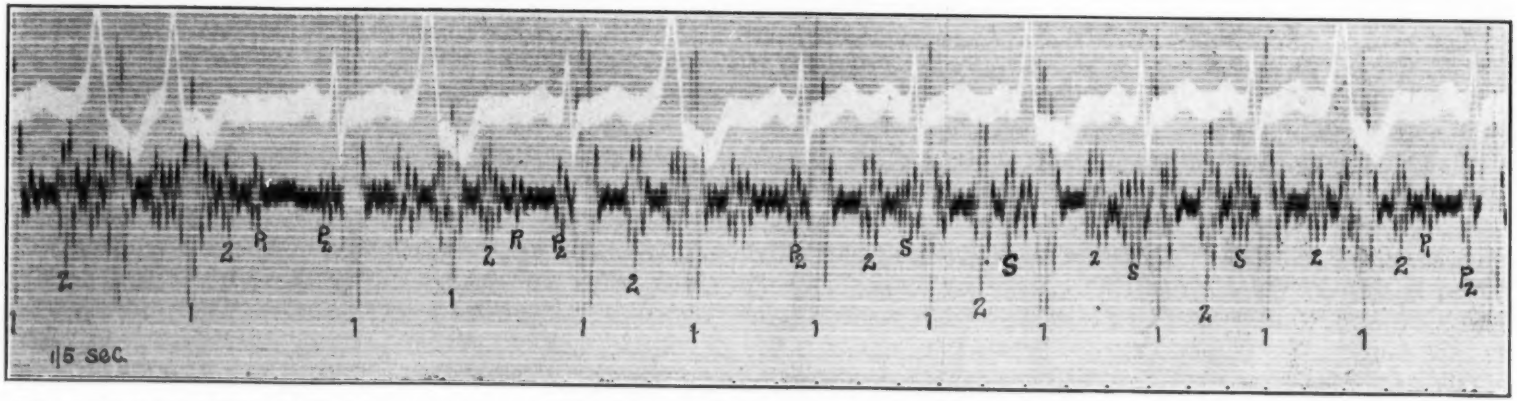

Fig. 9.—During regular rhythm, summation gallop (S) is present. During the compensatory pause following an extrasystole both a protodiastolic (P_1) and a presystolic (P_2) gallop sound are present.

superimposed on the protodiastolic zone. During auricular fibrillation in the three cases, only faint protodiastolic gallop sounds were heard irrespective of the cardiac rate or the length of the preceding heart cycle. (Fig. 5.)

3. Effect of Incomplete Heart-Block.—The effect of variation in position of auricular contraction on the intensity of gallop sounds was carefully studied in one case of incomplete heart-block. In this case the differences in loudness of gallop sounds in successive beats was striking. The sound tracings showed their time incidence to be in a range of 0.12 to 0.14 second after the second heart sound. When the P-wave began in a range of 0.02 second before to 0.02 second after the second heart sound, the gallop sound attained its maximum intensity. When the P-wave fell outside but near this zone, either before or after it, the gallop sounds were of moderate

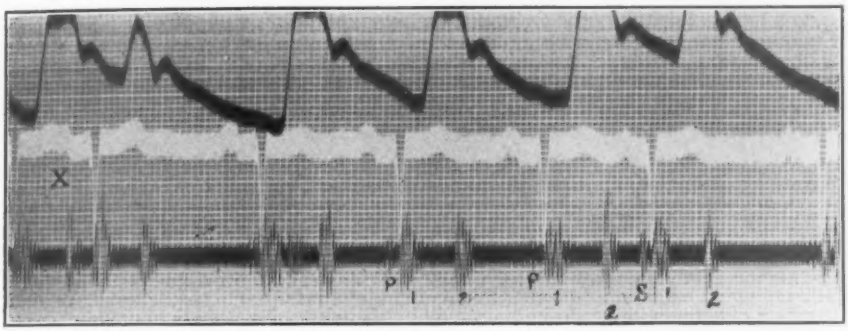

Fig. 10.—During regular rhythm, no protodiastolic disturbance is recorded, but there are small subsonic presystolic vibrations (p). In connection with certain premature auricular beats a single summation gallop sound (S) is recorded. When the auricular beat is highly premature (X), no gallop sound occurs, possibly because of curtailment of the protodiastolic phase.

intensity. When, however, the P-waves were far removed from the zone, the gallop sounds were comparatively faint. (Fig. 1.)

4. Effect of Ventricular Extrasystoles.—In three cases with rapid rates, loud gallop sounds and extrasystoles, the loud gallop sound failed to appear during the compensatory pauses succeeding premature beats, but in each case during such pauses there were present either protodiastolic or presystolic gallop sounds or both. On resumption of the rapid regular beating the loud gallop sound immediately recurred. Thus when auricular contraction was separated from the protodiastolic zone (as occurred during the compensatory pauses), the loud single gallop sound was replaced by less loud protodiastolic or presystolic sounds, or both. (Fig. 9.)

5. Effect of Auricular Extrasystoles.—In one case with auricular extrasystoles, there was present (while the rhythm was regular) a faint presystolic gallop sound, which began 0.14 second after the beginning of the P-wave. There was no protodiastolic gallop. When premature auricular beats occurred, there was a louder gallop sound which fell 0.14 second after the beginning of the aberrant premature P-wave and 0.20 to 0.23 second

after the beginning of the second heart sound. (Fig. 10.) In another case exhibiting auricular extrasystoles there was (during regular rhythm) a protodiastolic gallop sound, but the tracing also showed small waves (probably subsonic) at the time presystolic gallop might have been expected. When auricular extrasystoles occurred so that the premature auricular beats were superimposed on the protodiastolic period of the preceding beat, a loud gallop sound invariably occurred. Thus even the superimposition of an aberrant auricular contraction on a protodiastolic zone is capable of producing the summation phenomenon. (Fig. 11.)

It seems entirely probable that the summation effect influences the third heart sound in the same way that it does gallop rhythm, although little opportunity presented itself to test this point. In certain cases the third sound did not appear until the rate was rapid enough for summation to occur. In a young varsity oarsman with auricular extrasystoles, some transmitted and others blocked, the third sounds were heard and recorded only when the aberrant auricular beat fell in the range of ventricular

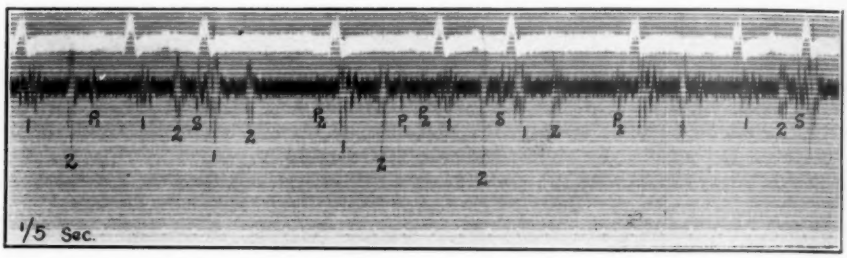

Fig. 11.—Protodiastolic (P_1) and presystolic (P_2) gallop sound vibrations (the latter subsonic) when beats are of normal type. Summation gallop (S) with vibrations of much larger amplitude when premature auricular beats occur.

protodiastole, irrespective of whether or not the extrasystole was blocked. Thus the mechanism was similar to that illustrated in Fig. 11.

From the above observations it is apparent that when auricular systole becomes superimposed on the protodiastolic zone of the preceding beat, a gallop sound may either appear for the first time, or if already present, become greatly intensified. This intensification occurs irrespective of whether the preceding gallop sound or sounds had been presystolic, protodiastolic or both.

The hypothesis of summation gallop is therefore consistent with the behavior of gallop rhythm under all the tests to which it was subjected. Furthermore, it appears to offer a rational explanation for some of the supposed vagaries of gallop rhythm (such as its comparatively frequent occurrence during tachycardia and during minor grade heart-block).

THE INCIDENCE OF THE VARIOUS TYPES OF GALLOP RHYTHM

The comparative frequency of the various types of gallop rhythm has been discussed by various writers, and statistics have been compiled based

on auscultatory findings. Not much confidence can be placed in these figures, not only because of unsatisfactory classification, but also because of the practical difficulty of accurate perception of time relations that presents itself in many cases without simultaneously recorded sound tracings and electrocardiograms.

Among our 60 cases, 14 showed only protodiastolic gallop while they were under observation and 22 only presystolic gallop. The summation form was recorded in 24. In 7 of these, due to constant tachycardia during the period of observation, no other manifestation of gallop was recorded. In the other 17, however, many of whom were under observation for extended periods of time, the findings were variable. When the rate slowed so that summation was no longer present, one of the following was recorded: (1) no gallop sound; (2) presystolic gallop alone; (3) protodiastolic gallop alone; or (4) both presystolic and protodiastolic gallop. It is of interest that in 13 of the 17 cases, both presystolic and protodiastolic gallop were recorded (occurring either together or singly at various times). Analysis of all our tracings in the 60 cases revealed the fact that at one time or another 29 had protodiastolic gallop and 37 presystolic gallop.

Although the number of cases studied is far too small for statistical purposes, the figures appear to indicate that there is no great difference of incidence between protodiastolic and presystolic gallop. Previous studies are contradictory regarding this point. Thus recently it has been stated that "when differentiation is possible, it is found that the protodiastolic gallop rhythm is much more common than any other timing, being perhaps six times more common than the presystolic type while the mesodiastolic type is rarer still than the presystolic. . . . ."[13] Other writers believe that presystolic gallop is more common than protodiastolic.

The unmistakable tendency for both presystolic and protodiastolic gallop to occur in the same case deserves emphasis. Isolated case reports of this association are available in the literature. The fact, however, that in 13 of our 60 cases both protodiastolic and presystolic gallop were recorded establishes the close relationship between these two. Furthermore, it seems probable that if our studies of the various cases had been extended over longer periods of time, more might have shown this association.*

Among the 10 cases classified as having the physiological third heart sound, the third sound was protodiastolic in 9, a presystolic sound was heard in only 1 case, despite the fact that small presystolic vibrations were registered in several.

RIGHT-SIDED GALLOP RHYTHM

Potain[2, 14] was the first to describe right-sided gallop rhythm. He pointed out that in right-sided gallop, the gallop sound is heard best, not at the apex, but in the neighborhood of the xyphoid cartilage. Potain associated

*These observations tend to support Potain's view that the various types of gallop rhythm are closely related.

right-sided gallop rhythm with dilatation of the right side of the heart and tricuspid insufficiency, but believed that the underlying disease causing right-sided cardiac dilatation was usually "gastro-hepatic." He also stated that it tended to occur in patients with chlorosis.

Several cases of right-sided gallop have been reported since Potain's original observations, but some writers still believe that it is unsafe to state that right-sided gallop can be distinguished from left-sided gallop. Pezzi[15] believes that the usual gallop is in all probability produced in both sides of the heart.

Among our 60 cases which exhibited gallop rhythm, the localization was always right-sided in 3, and sometimes right-sided and sometimes left-sided in two. In 3 of the 5 cases the extra sound was protodiastolic; in one it was sometimes protodiastolic and sometimes presystolic; while in one, summation gallop was present. The patient with right-sided summation gallop had advanced pneumoconiosis and right-sided heart failure. At necropsy the right ventricle was found to be greatly dilated and the left ventricle little if any changed in size. In one of the two cases with only right-sided protodiastolic gallop, a clinical diagnosis of right-sided heart failure was made because of severe congestive phenomena from which, however, the lungs seemed to be spared. The other had hyperthyroidism, auricular fibrillation and a very rapid ventricular rate. In this case, however, we were unable to determine whether there was disproportionate damage on the two sides.

The two patients who exhibited both right and left-sided gallop were in states of profound decompensation. One, during a short period, exhibited both right and left-sided gallop simultaneously. The other patient exhibited left-sided gallop for a time, then right-sided gallop and finally left-sided gallop again. During the period that right-sided gallop was present, there was no pulmonary congestion discoverable but there was marked engorgement of the veins of the neck, congestion of the liver, and edema, this clinical picture suggesting a predominately right-sided heart failure. At necropsy both the right and left ventricles were found greatly dilated.

These observations have left no doubt in our minds that there is a type of gallop rhythm which may properly be termed right-sided. This is based on (1) auscultatory localization of the gallop sound, (2) the fact that the localization can be confirmed by sound registration studies, and (3) the occurrence of predominantly right-sided heart failure in cases exhibiting the right-sided localization of the sounds.

On the basis of the present status of our knowledge regarding physiological third heart sounds and gallop rhythm the following schema of classification is proposed:

SCHEMA OF CLASSIFICATION

1. *Physiological Third Heart Sounds.*—(Occur commonly in children and young adults with no evidence of cardiovascular damage nor signifi-

cant alteration in cardiac function. The sounds are characteristically dull, low-pitched, and are heard best near the apex.)

(a) Protodiastolic.—Fall in the protodiastolic time zone, usually beginning 0.12 to 0.21 second after the beginning of the second heart sound. Nearly all cases belong to this group.

(b) Presystolic.—Bear a definite relation to auricular contraction. Begin 0.08 to 0.14 second after the beginning of the P-wave of the electrocardiogram. While small vibrations are commonly found in sound tracings, it is only rarely that sounds can be heard.

(c) Summation Form.—Occur only when time zones of protodiastolic and presystolic sounds are merged because of tachycardia, sinus arrhythmia or auricular extrasystoles.

2. *Gallop Rhythm.*—The term "gallop rhythm" is to be applied only when there is evidence of cardiovascular damage or significant alteration in cardiac function. The sounds are characteristically dull and low-pitched. Gallop sounds are usually left-sided and are heard best over or near the apex, but occasionally may be right-sided and heard best near the xyphoid.

(a) Protodiastolic.—Fall in the protodiastolic time zone usually beginning 0.12 to 0.21 second after the beginning of the second heart sound. Usually left-sided but occasionally right-sided.

(b) Presystolic.—Bear a definite relation to auricular contraction. Begin 0.08 to 0.14 second after the beginning of the P-wave of the electrocardiogram.* The right-sided type is very rare.

(c) Summation.—Occur only when the time zones of protodiastolic and presystolic gallop sounds are merged, because of tachycardia, heart block, sinus arrhythmia or auricular extrasystoles.

We believe that the above modification of Potain's classification has the following advantages:

1. The so-called mesodiastolic gallop is discarded, since no justification has been found for it as an entity apart from protodiastolic and presystolic

*In a recent paper Duchosal[11] has discussed the time relations of the P-waves of the electrocardiogram and auricular (presystolic) gallop sounds. Since the values which he reports differ considerably from those obtained by other workers, including ourselves, it becomes necessary to analyze such evidence as is available in the attempt to account for this discrepancy. Thus Duchosal, measuring from the *peak* of the P-wave to the beginning of the gallop sound, found the range of these intervals to be −0.02 to +0.14 second. Since the peak of the P-wave usually falls 0.03 to 0.06 second after the beginning of the P-wave, it is obvious that Duchosal's range of values is much wider than ours. This is of special interest in connection with the short intervals, since Duchosal believes that these have a bad prognostic significance. In his paper we find five figures to illustrate extremely short intervals between the peak of the P-wave and the gallop sound. In his Figure XI, the only one of the five in which the vibrations regarded as auricular (presystolic) gallop are not open to a question of interpretation, the time relations are within conventional limits, the interval between the beginning of the P-wave and the gallop sound being 0.08 second. In his Figure IV the interval is also 0.08 second, but since the gallop sound falls only 0.16 second after the second sound it is also within the range of protodiastolic gallop. In his Figure X, the vibrations regarded as representing gallop fall only 0.04 second after the beginning of the second sound. Even with the most extreme grades of tachycardia, the interval is rarely less than 0.12 second, and in our experience has never been less than 0.10 second. The interval of 0.04 second would therefore have to be regarded as almost impossible for gallop rhythm although well within the range of a split second sound. In his Figures XII and XIII in which the time intervals between the beginning of the P-wave and the gallop sounds are very short (in Figure XIII only 0.02 second) the time relations to the second sound correspond to what is expected in protodiastolic gallop. Thus in our opinion Duchosal has not demonstrated the existence of very short time intervals (less than 0.08 second) between P-waves and presystolic or auricular gallop sounds.

gallop. A source of confusion in the understanding of gallop rhythm and its classification has therefore been removed.

2. The hypothesis of summation is in accord with all known facts regarding gallop rhythm and the physiological third heart sound. Its use makes classification sharply definitive, so that there is no difficulty in fitting cases into their proper categories. Furthermore, certain of the supposed vagaries of gallop rhythm are reasonably accounted for by this hypothesis.

DIFFERENTIAL DIAGNOSIS

The characteristics of gallop rhythm and the physiological third heart sound which have been described above are sufficiently distinctive to make possible their differentiation from all other groupings of heart sounds. In the great majority of cases purely clinical methods are adequate, no apparatus except a stethoscope being required. It is necessary to pay attention to the localization of sounds, their pitch, duration, and timbre. For these purposes, auscultation is far superior to any of the sound registration devices now available. In addition the examiner should educate himself to some appreciation of the differences in duration of short intervals. Accurate timing by graphic methods, although a satisfactory procedure, is necessary for diagnosis in only a small minority of cases.

In our experience the following sounds have been confused with either gallop or physiological third heart sounds:

(1) The opening snap of mitral stenosis; (2) mid-diastolic murmur; (3) presystolic murmur; (4) reduplicated first heart sound; (5) reduplicated second heart sound.

(1) We have recently reported a study of the characteristics of the opening snap in mitral stenosis.[3] It is differentiated by the following: (a) It occurs only in mitral stenosis, whereas gallop rhythm is very rare in mitral stenosis and does not occur if the stenosis is well developed. (b) It is a short, sharp sound. (c) Its point of maximum audibility is in the third or fourth interspace over the body of the heart and not at the apex. (d) It tends to fall closer to the second sound, although the longest intervals overlap the shortest intervals in gallop rhythm or the physiological third sound. There is, however, a fundamental difference in time relations since the opening snap occurs before ventricular filling has begun; whereas gallop and third sounds always fall near the summits of waves of ventricular filling. Occasionally the diagnosis cannot be decided by clinical methods. Under such circumstances a simultaneous record of heart sounds and apex cardiogram will be necessary for differentiation.

(2) Mid-diastolic murmurs sometimes occur in mitral stenosis when the rate is rapid. On superficial examination these may simulate the summation type of gallop rhythm. However, the utilization of the various methods for influencing gallop sounds and diastolic murmurs (changes in position, cardiac rate, exertion) usually makes differentiation possible.

The gallop sound retains its characteristics, particularly that of being fairly quickly damped, although its loudness may change considerably, whereas the murmur tends to be prolonged and has a decrescendo quality. Furthermore, gallop sounds are heard best nearer the apex than the murmurs of mitral stenosis. In doubtful cases the presence of other signs suggesting mitral stenosis is strong presumptive evidence for the murmur. Simultaneous graphic records of sounds and apex cardiogram show that the murmur of mitral stenosis begins at the onset of ventricular filling rather than at the summit of the wave.

(3) In several of our cases, presystolic gallop sounds were mistaken for presystolic murmurs of mitral stenosis. In no instance was a presystolic murmur mistaken for gallop. The presystolic gallop is a low-pitched short sound usually clearly separated from the first sound (unless the A-V interval is very short), whereas presystolic murmurs tend to be longer in duration and crescendo in quality running up to the first sound. The differentiation can usually be made by the auscultatory characteristics including localization of the sounds, but the presence or absence of associated signs of mitral stenosis is also an important differential point.

(4) The clinical differentiation between presystolic gallop and reduplication of the first heart sound is occasionally difficult and in certain cases impossible. The quality of sounds and location do not offer dependable criteria for differentiation. The time relations are most important. Thus in some cases it can be determined that the sound is actually presystolic, coming before ventricular contraction. Another point of value is the interval between sounds. In reduplication of the first sound, this interval does not tend to exceed 0.07 second even in cases of bundle-branch block. In most cases of presystolic gallop rhythm, the intervals range between 0.08 and 0.14 second. When A-V conduction defects are present, the intervals are still longer. If, however, the P-R interval is short (0.12 to 0.14 second) the split between the gallop and first heart sound may be no wider than that of reduplicated first sounds. Thus a wide split between sounds constitutes strong evidence for gallop rhythm; a narrow split has no value as a differential point. Under these circumstances a simultaneously recorded sound tracing and electrocardiogram may be necessary for a decision.

(5) Reduplicated second sounds are easily differentiated from protodiastolic or summation gallop rhythm and physiological third sounds by the following characteristics: (a) Reduplication of the second sounds may occasionally be well heard at the apex, but its maximum audibility is at the base and rarely as low as the fourth interspace. (b) Second sounds are shorter, sharper and higher in pitch than gallop sounds. (c) The intervals between the two components of split second sounds are appreciably shorter than those between second sounds and gallop rhythm.

There are three other types of sound which should be mentioned in the

differential diagnosis. These are (a) pericardial frictions; (b) the rather common clicking sounds which fall between the first and second heart sounds,* and (c) the so-called systolic gallop sounds. Friction sounds are differentiated by their characteristic rough or scratching quality and the fact that they are usually heard both in systole and in diastole, tending to be loudest during systole. Systolic gallop and the systolic clicking sounds both fall between the first and second heart sounds. The clicking sounds have no resemblance to gallop sounds, and the differences in quality are sufficient to differentiate them. Systolic gallop sounds, however, are similar in quality to the types of gallop which occur during diastole. Their occurrence during systole and the fact that they are heard best over the aortic area clearly differentiate them.

SUMMARY

1. The only available criterion for distinguishing between physiological third heart sounds and gallop rhythm is the status of cardiac function. Both types of sound are accentuated by the same procedures. They have similar time relations, quality and intensity. Their positions of maximum audibility are identical except that right-sided physiological third heart sounds are unknown.

2. Gallop and physiological third heart sounds invariably fall in either the protodiastolic or the auriculosystolic time zone.

3. When these two time zones become superimposed, either as a result of tachycardia, minor grade heart block, sinus arrhythmia or auricular extrasystoles, gallop sounds may either appear for the first time, or, if already present, become markedly accentuated. This effect is so pronounced as to constitute a summation phenomenon.

4. The hypothesis of summation is in accord with all known facts regarding gallop rhythm. Moreover, it offers a reasonable explanation for some of the variations in gallop sounds hitherto unaccounted for.

5. A classification of physiological third heart sounds and gallop rhythm, based on Potain's classification of gallop rhythm, but altered to correspond with objective phenomena, is proposed. The erroneous concept of mesodiastolic gallop is discarded, and summation gallop is recognized. The classification abolishes the practical difficulties, heretofore encountered so frequently, in placing cases into proper categories.

6. There appears to be no great disparity in the incidence of presystolic or protodiastolic gallop. Summation gallop is little if any less frequent. It can be produced in cases with either of the other types of gallop, or in cases with a predisposition to gallop, by the simple expedient of accelerating the cardiac rate enough to bring about superimposition of protodiastolic and presystolic events.

7. Potain's conception of right-sided gallop rhythm, disputed by certain

*We have designated these sounds "mid-systolic clicks."

observers, has been confirmed by our investigations. It tends to occur in cases exhibiting predominantly right-sided heart failure.

8. In the differential diagnosis of gallop rhythm and the physiological third heart sound, errors have been encountered involving one or another of the following: (1) the opening snap of mitral stenosis; (2) mid-diastolic murmur; (3) presystolic murmur; (4) reduplicated first heart sound; (5) reduplicated second heart sound. Other possible sources of error are (a) pericardial friction sound; (b) mid-systolic click; and (c) the so-called systolic gallop rhythm. In the great majority of cases differentiation is possible by clinical methods alone. In occasional cases, however, accurate timing requiring graphic methods is necessary.

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P-WAVE CHANGES IN ACUTE CORONARY ARTERY OCCLUSION*

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CHANGES in the P-wave of the electrocardiogram during an attack of acute coronary artery thrombosis seem not to have been reported. That a definite change occurs, however, in the auricular complex will be demonstrated by a review of the last forty cases treated at the New York Hospital, New York. A typical example will illustrate these changes in the P-wave.

CASE 1. (301,532) A Greek, forty years of age, was admitted to the New York Hospital at 10 P.M., October 11, 1931, for severe precordial pain. That day, about one hour after his lunch, the patient commenced to have precordial pain which radiated to the back and down the left arm to the finger tips. He rested in bed, his symptoms abated, and after supper he went for a walk. The pain suddenly returned with great severity, and he immediately took a taxicab to the hospital. The physical examination on admission revealed a well nourished and well developed individual "writhing and twisting with pain" and with a cyanotic grayish color. The heart was regular, the rate 66 beats per minute, and the heart sounds were faint. The patient was very sick. He was dyspneic, the precordial pain was marked, sweating was profuse, the lungs were congested at the bases, the patient coughed. Because of the severe precordial pain, morphine sulphate was administered in one-fourth grain doses every four hours until the fifth day after admission when only one dose was given. On the sixth day the patient was definitely better, but there were still some pain, sweating and restless sleep. The next day was his first "comfortable day." The temperature on the day of admission was 99° F., on the third day it was 103° F., and then it gradually fell to 99° F. on the eleventh day. The pulse rate corresponded to the temperature, ranging from 120 beats per minute on the third, to 60-70 per minute on the ninth day. The blood count on the third day in the hospital disclosed a leucocyte count of 15,300 with a polymorphonucleosis of 81 per cent, but on the seventh day the count was normal. The blood Wassermann test was negative. The urine was normal. On the day after admission the blood pressure was 100/80 mm. Hg, and at the time of discharge from the hospital it was 120/70 mm. Hg. A teleroentgenogram of the chest, which was taken October 16, 1931, the sixth day, showed an enlarged heart with a concentrically hypertrophied left ventricle, and showed also signs of chronic passive congestion in the lungs. On November 4, 1931, in a second film, the lungs were clear. The patient convalesced uneventfully and was discharged from the hospital on November 6, 1931, with the diagnosis of thrombosis of the coronary artery.

The first electrocardiogram was taken October 13, 1931, less than forty-eight hours after admission. It showed a normal sinus rhythm, rate about 100 beats per minute (Fig. 1). The voltage of the QRS group was moderately low. The striking features were the abnormal S-T intervals and the large P-waves. In subsequent records the rate became slower, the voltage of the QRS gradually higher, the T-waves in Leads I and II became

*From the Cardiographic Laboratory, New York Hospital, New York.

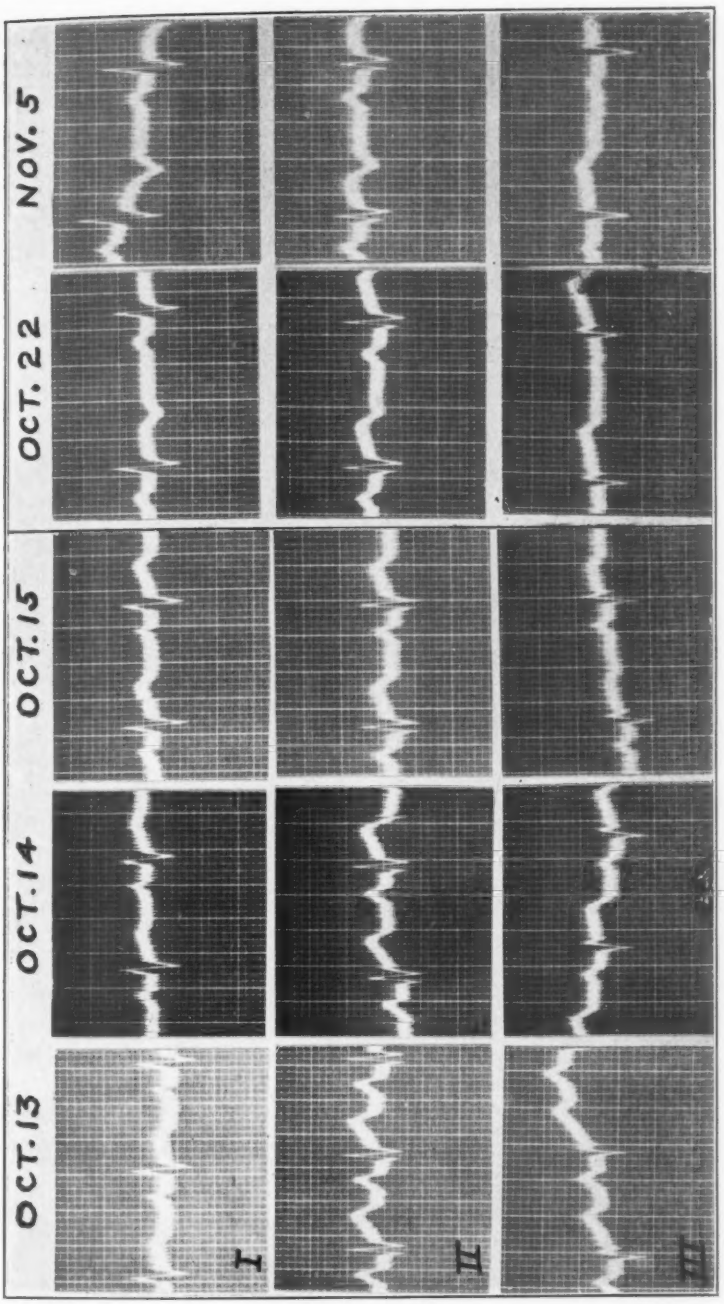

Fig. 1.—Attack of acute coronary artery occlusion October 11, 1931. Note large P-waves on October 13, the third day of illness. On October 14, P-waves practically unchanged. On October 15, fifth day, P-waves return to normal size and remain so until discharge from hospital November 5, 1931.

inverted and the S-T intervals normal. The P-waves remained large for three days and then gradually diminished, reaching a fixed size about the fifth day (Fig. 1).

In 32 cases out of the 40 studied there were similar changes in increased size of the P-waves during the early days of the acute coronary artery thrombosis (Table I). The P-waves were not only relatively enlarged but

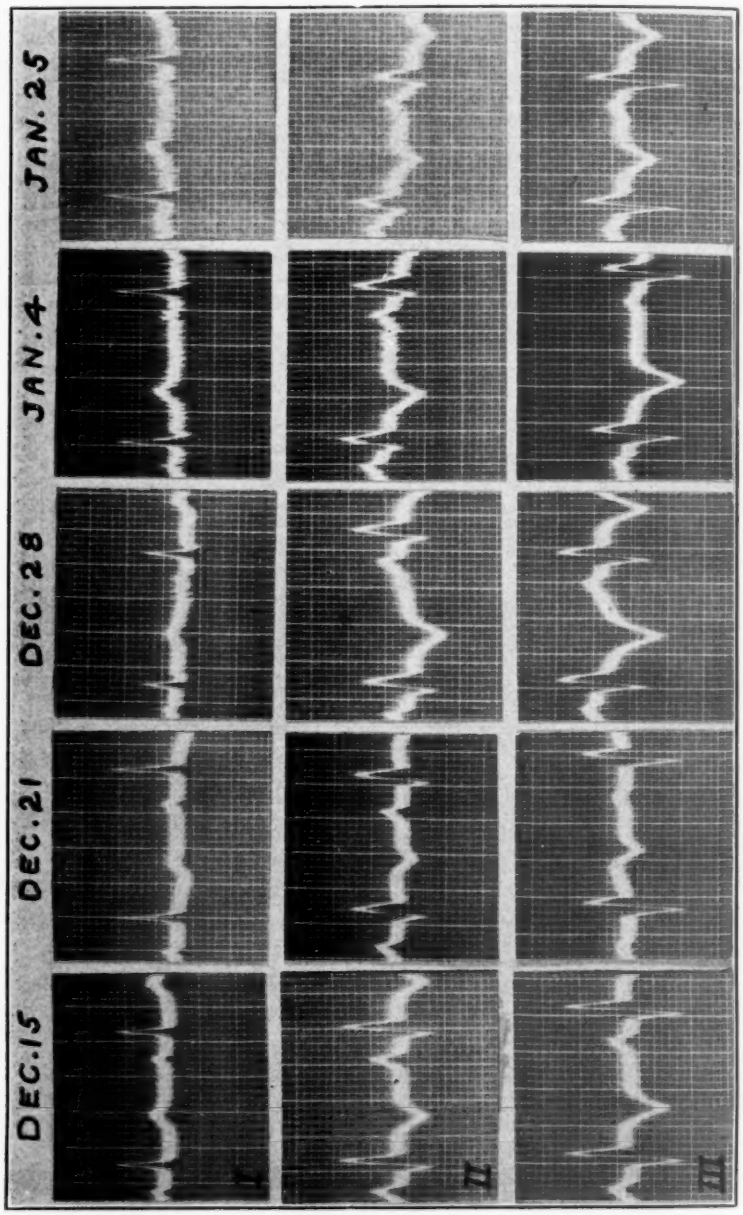

Fig. 3.—Attack of acute coronary artery occlusion December 13. Large P-waves December 15, the third day of the attack. P-waves return to normal size on December 21, the ninth day.

often absolutely increased as well. In normal individuals the P-wave is under 2 mm. in height in any lead. Lewis and Gilder[1] in 52 normal people found that the P-wave was never 2 mm. high; i. e., the maximum was

1.7 mm., and the average height of the P-wave was 1.16 mm. in Lead II, the derivation in which it was highest. Pardee[2] considers a P-wave of 2 mm. or more to be abnormal. In a series of 250 normal individuals on whom we took electrical tracings at Cornell University Medical College, only eight individuals had auricular complexes of 2 mm. height (3 per cent), whereas among the forty patients under consideration there were actually sixteen individuals whose P-waves measured 2 mm. or more in the first days of their illness, a percentage of 40 (Table I).

It is felt that, unlike the P-wave in mitral stenosis, the auricular complex in acute coronary artery thrombosis varies primarily in amplitude. It is usually a sharply peaked wave (Figs. 1 and 2). Occasionally, however, the P-wave becomes wide and notched or has a double summit. In four of our patients notching occurred; in two cases the P-wave became both wide and notched. In only one of these six cases was the amplitude increased. These variations occurred during the early days of the coronary artery closure, just as did the variations in size.

Not only is the maximum amplitude of the P-wave in acute coronary artery closure of interest, but also it is instructive to follow the variations in size or shape which occur in a series of electrocardiograms of the same individual (Table I). It has been found that beginning often on the very day of onset of the acute coronary artery closure and continuing to about the third, fourth or fifth day thereafter, the P-wave has the largest amplitude, and that from about the sixth day on the P-wave returns to normal. These figures and those that follow must not be taken too literally, for in many of the cases tracings were taken not daily but rather every other day, and occasionally there were no records for the first few days of the illness.

The P-waves were larger at a time when there was clinical and electrocardiographic evidence of acute coronary artery closure with severe circulatory embarrassment. Table I shows the times of appearance of the increase in the size of the P-wave, of its recession to normal, of RS-T changes, T-wave inversions, and also the days on which proof was obtained of severe myocardial and circulatory failure (such as congestion in the lungs, cyanosis of finger tips or lips, liver enlargement, severe dyspnea or orthopnea). Systolic blood pressure below 100 mm. Hg, considerable precordial or chest pain, leucocytosis (10,000 white blood cells, or more), fever (100° F. or more), are also listed. The day on which the coronary artery accident occurred is tabulated as 1 and hence the Arabic numerals on the chart indicate time in days in relation to this first day.

The records seem to show that if severe circulatory failure is present, as indicated by cyanosis, congestion of the lungs, enlarged liver, etc., then the size of the P-wave will be found greater than that seen at the time when physical signs or laboratory tests show recovery from acute circulatory failure. In the table the first 16 cases are those that had P-waves of 2 mm. or more and every single one of these shows this relationship. In the remaining 24 cases (Nos. 17 to 40) circulatory failure was found 20 times,

TABLE I

P-WAVE CHANGES IN ACUTE CORONARY ARTERY OCCLUSION RELATED TO CLINICAL OBSERVATIONS*

CASE NO.	NAME	AGE	SEX		MAXIMUM SIZE P-WAVE IN MM.	LARGE P-WAVE	NORMAL P-WAVE	RS-T CHANGES	T CHANGES	LUNG CONGESTION		LUNGS CLEAR	LIVER LARGE	CYANOSIS LIPS FINGERS	SEVERE DYSPNEA ORTHOPNEA	LOW BLOOD PRESSURE	SEVERE PAIN	FEVER	LEUCOCYTOSIS	MISCELLANEOUS
			F	M						PHY. SIGNS	X-RAY									
1	J. Br.	56		V	2.5	1-4	6	1-3	4-6	1							1	4, 15	1, 2	
2	E. Ca.	40		V	2.5	3	5+	3-12	12		6	25		1	1		1, 4	2-9	3	
3	E. Eb.	51		V	2.0	1-3	11	1-3	11	1	1			1	1	3, 4, 18	1	1-20	1-17	
4	N. Fi.	53		V	2.0	3-8	9-10		7	1				1	1	1	1	2	1, 2	
5	N. Fr.	52		V	2.2	2-7**	8+		1+		1			1		4	1	2-19	1, 23	
6	D. Go.	52		V	2.8	1-9	82	3-9	3-9	1					1		1	2-6	2	
7	C. Ha.	39		V	3.0	3-5	9-40	3-8	3+					1	1	4, 20, 28	1, 2, 3	2-8	1-17	
8	J. Ha.	50		V	2.1	3-5	6+	3-5	6	1				1	1-2	5, 9, 12, 14	1, 2	19, 27, 29	1	
9	J. La.	51		V	2.0	1-5	9	1-9	1-9	1					1		1	2-7		Pt. died
10	R. Mo.	49		V	2.0	5-7								1	1		1	1	1-9	
11	B. Ro.	47		V	2.0	4	8	4-8	8+	6						16	1	4-7	5, 46	
12	H. Ro.	58		V	2.0	3-7	20+	3-10	3+		7-35			2			2, 3	3, 35	3-41	
13	L. Ru.	43		V	2.2	1-5	13-37	1-3	3+	1				1	1	5-6	1, 5	2, 7, 39	1, 6, 38	
14	S. Se.	47		V	2.9	2-3	6	2-3	2	1	6		5	1		1	1	1-14	1, 3, 10	
15	D. Sh.	58		V	2.0	1-7**	10, 46	1-7	5+	1	1				2	6	1	2, 7	1	
16	H. St.	57		V	2.0	3	5	1-14	11		2		1	1		3-29	1, 3, 14	2-16	1-24	
17	J. Ba.	42		V	1.3	1 **	3	1	3+	1	2, 7	9	2	1	1	8	1, 2, 3	2-10	1-13	
18	M. Br.	46		V	1.7	1-6		1+	3	1	2, 20				4, 18	3-17	1-20	1-21	1-21	Pt. died
19	C. Co.	51		V	1.0				5+	3	5		2		1		1	3-8	5, 7	
20	E. De.	78	V		0.8				1+								1	2-7	1	

*The day on which the acute coronary artery occlusion occurred is considered the first day and is tabulated 1, the second day of illness 2, the third 3, etc.

**In these cases the change in the P-wave was a notching or double summit, not an increase in size.

TABLE I (CONTINUED)

CASE NO.	NAME	AGE	SEX		MAXIMUM SIZE P-WAVE IN MM.	LARGE P-WAVE	NORMAL P-WAVE	RS-T CHANGES	T CHANGES	LUNG CONGESTION		LUNGS CLEAR	LIVER LARGE	CYANOSIS LIPS FINGERS	SEVERE DYSPNEA ORTHOPNEA	LOW BLOOD PRESSURE	SEVERE PAIN	FEVER	LEUCOCYTOSIS	MISCELLANEOUS
			F	M						PHY. SIGNS	X-RAY									
21	J. De.	45		V	1.9	4-6**		3-9	12	1					1	5-20	1-4	2-8	1-7	
22	E. Fe.	41		V	1.5	4-9	18	4-9	4+	1	4			1	1, 9, 16	18, 24, 26	1	1-4	2	
23	J. Fl.	45		V	1.8	3-6	29	3-7	6+		3						1, 2, 3	3-11	3-17	
24	R. Ga.	64		V	1.4	3-5	13	3-7	14+	3		4		1			1, 2, 3	3-8	3-20	
25	H. Gr.	40		V	1.0				2								1	2-7	2	
26	J. Ha.	45		V	1.6	3 **	4	2	3-4					1	1		1	2, 3, 4	2, 3, 4	
27	F. He.	69		V	1.0			5-12	12	3	3						1	3-31	4, 6, 12	
28	J. Ho.	51		V	0.9			3-8	4	2						2, 19	1	2-23	2-7	
29	H. Ja.	43		V	1.5				2+		3						1-43	3-60	3, 9, 10	
30	H. Kn.	43		V	1.4	3	18	3	3	4	11			3	4		1	3, 5	3, 6	
31	T. Lu.	45		V	1.4	4	8+	3-5	11	3		5		3	1, 2	1, 14, 20	1, 2, 17	3-19	3, 5, 13	
32	W. Ov.	58		V	1.7	1-8	9+	2-8	10	1				1	1			-	5, 7	Pulmonary Edema 1
33	M. Pr.	56		V	1.8	3-9	10+	2-10	12	1	2-6				1		1	1-30	1, 3, 23	
34	J. Rh.	55		V	1.4	2-7	11	2	6						1		1	2-24	2, 16	
35	M. Ro.	43		V	1.6				2+					1		1-32	1, 3, 5	2, 5, 6	2, 4, 29	
36	C. R.	—		V	1.5	1-2**	4-15	1-15	15								1	2-7	3-13	
37	W. Sc.	66		V	1.8				13	1						3-12	1, 2	2, 26	1-12	
38	S. Tu.	35		V	1.9	1-6	16+	2-6	3+			32					1	2-6	2, 5, 33	
39	L. We.	43		V	1.9	3	7	3+	7		1		1	1			1	2-10	1-23	
40	J. Wo.	53		V	1.2	2-9	9+					31		1		1, 13, 14, 17	1		1, 2	

and corresponding to this there were changes in the P-wave in 14 of these 20 cases. Hence all together there were 36 patients in whom circulatory failure was evident, and in 30 of these (83 per cent) P-wave changes were recorded.

It is interesting to review the six cases in which there was no change in the P-wave to correspond to the clinical finding of circulatory failure. In case No. 19 (C. Co.) only four records were taken; whereas the average for each patient for the entire series of 40 was nine. In case No. 27 (F. He.) there were no tracings for the first five days. Hence there remain 4 cases, i. e., No. 28 (J. Ho.), No. 29 (H. Ja.), No. 35 (M. Ro.), and No. 37 (W. Sc.) for which no explanation can be offered for the absence of change in the P-wave of the electrocardiogram.

The change in the size (or shape) of the P-wave was associated not only with clinical signs of acute coronary thrombosis but with the electrocardiographic signs as well. RS-T abnormalities occur immediately after an acute coronary artery closure and usually last for a few days. They recede about the time T-wave inversions appear. In this study 30 cases with striking RS-T deviations were found, and in 28 of these the P-wave was larger while these were present than during the period when T-wave inversions appeared.

The P-wave was largest in Lead II in practically all of our cases. The P-wave was also prominent in one other lead but to a smaller extent, so that the variation in this wave was evident in combinations of Leads I and II, or Leads II and III. Twenty times the P-wave was most prominent in Leads I and II and on 11 occasions in Leads II and III.

Further details of the electrocardiographic changes were as follows: Abnormal T-waves were present in all cases but two, and were the most common of all the changes found in these cases of acute coronary artery closure. RS-T intervals were abnormal in 30 patients; QRS waves alone in 16 patients; P-R intervals, i. e., prolongation of the auriculoventricular conduction 9 times; large Q-waves in Lead III 8 times. A left axis deviation (left ventricular preponderance) was observed 23 times, a right axis deviation (right ventricular preponderance) 3 times.

The average age of all our patients was fifty years. There was only one female in the entire series.

DISCUSSION

It is very surprising that there should have been no description of the P-wave in acute coronary artery occlusion. A cursory glance at the illustrations used by authors[3, 4] who have made comprehensive reviews of the subject of acute coronary artery thrombosis will show numerous examples of high voltage P-waves.

The mechanism of production of the increase in size in the P-wave in these cases requires explanation. This increase may be due to change in position of the auricles or perhaps due to a transient enlargement of these

chambers. However, there was usually no change in axis deviation of the ventricles, nor in the size of the QRS complexes, and these are usually altered with change in heart position. Again, if rotation of the auricles occurred, one might expect an inversion of the P-wave as occurs, for example, in Lead III of the electrocardiogram in obese patients where the diaphragm is elevated.

There is a strong possibility that the enlarged P-wave represents auricular dilatation and perhaps hypertrophy. After closure of a coronary artery the auricle has a greater function to fulfill, since the ventricle is injured. This seems the more plausible when one recalls what happens in the heart of a dog after a coronary artery has been ligated. The involved area of the ventricle is practically paralyzed, it becomes cyanotic and dilated, the ventricular contractions are feeble.

Another explanation may be that increased intra-auricular pressure produces auricular dilatation. With the fall in systemic pressure a stasis may occur in the great veins of the neck, and the auricles, being in intimate pressure and volume relations with them, will sustain a rise in the intra-auricular pressure, and dilatation of these chambers will follow. Clinical experience supports this theory, for the large P-waves appear when there are signs of venous engorgement such as large tender livers, dilated cervical veins, congestive râles at the lung bases.

There were only eight patients among the forty in whom there were no changes in the size of the P-wave. Only a variation of at least 0.5 mm. was considered a change. Considering the limits of an investigation of this sort and considering that 32 cases out of 40 showed variations in size, and occasionally in the shape of the P-wave, and that these changes corresponded to and varied with the clinical (83 per cent) and electrocardiographic findings (93 per cent) that occur in acute coronary artery closures, it is felt that the P-wave abnormalities are a result of changes produced in the auricle or auricles by the acute coronary artery thrombosis. The left auricle is probably the chamber most frequently affected, since the left ventricle is most often injured. Perhaps this is the reason the P-wave changes occur more frequently in Leads I and II than in Leads II and III.

The P-wave changes have been found very helpful in making an electrocardiographic diagnosis of coronary artery occlusion. Very frequently, single equivocal tracings, as for example, one showing iso-electric (flat) T-wave in Lead I, will suggest a coronary artery accident if a big P-wave is present.

In the table the headings "large P" and "normal P" indicate that at first the P-wave is larger than normal and that when it becomes smaller it reaches its usual size. However, no direct proof has been adduced to show that the P-wave in the first few days of an acute coronary artery occlusion is larger than the individual's P-wave before the accident to his heart. Since, however, the P-waves of 2 mm. or more occurred in a much higher percentage than normally, it seems reasonable to believe that these are

abnormally large P-waves for these patients and that the subsequent smaller size of the P-waves is probably their normal size. Using the same reasoning on the 24 cases in which the P-wave was never 2 mm. in size, it seems logical to assume that this wave in the early days of illness is relatively large and that later when it becomes smaller it reaches the normal for the patient. In the table, then, the word "large" signifies either a relative increase in size of the P-wave or a relative and absolute increase, and the word "normal" refers to its subsequent smaller size.* In some five or six private cases in which electrocardiograms were available before the acute coronary artery thrombosis took place it was clearly apparent that the first P-waves were relatively or absolutely increased in size and the subsequent smaller waves were a return to normal size.

SUMMARY

In 40 cases of acute coronary artery occlusion definite changes in the P-waves occurred in 32 patients (80 per cent). These changes consisted for the most part in increase in amplitude of the P-wave of at least 0.5 mm. and occasionally in notching or widening of the auricular complex. In 16 patients (40 per cent) the P-waves measured 2 mm. or more in height in some lead.

The change occurred more frequently in Leads I and II rather than in Leads II and III, but always in Lead II. It is suggested that P-wave changes in Leads I and II are associated with left auricular dilatation.

The P-waves were larger in the first few days of acute illness when cyanosis, congestion of the lungs, enlarged liver, severe dyspnea or orthopnea were present, and became smaller when there was recovery from circulatory failure. The P-waves were larger when RS-T changes were present and returned to normal when T-wave inversions appeared.

There is evidence that the larger P-wave early in acute coronary artery disease is indicative of a dilated auricle, and it is suggested that this chamber takes over a portion of the work of the injured ventricle.

The increase in size or the change in shape of the P-wave is one of the electrocardiographic signs of acute coronary artery occlusion.

I am indebted to Dr. Harold E. B. Pardee for his interest in this study and for many valuable suggestions.

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*Strictly speaking the word "large" should be restricted to P-waves of 2 mm. or over, as it has been done in the body of this article, but not necessarily so in the table.

CLINICAL OBSERVATIONS ON THE DYNAMICS OF VENTRICULAR SYSTOLE

IV. Mitral Insufficiency and Mitral Stenosis*

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THE recent reports of experimental studies of the cardiodynamics of acute and of chronic mitral insufficiency[1, 2] and of acute and of chronic mitral stenosis[2, 3, 4] have made desirable a correlation of the clinical with the experimental findings in these valve lesions. With this objective this clinical study was made.

MITRAL INSUFFICIENCY

Dynamically, mitral insufficiency caused by rheumatic scarring has long been recognized as a benign lesion (Mackenzie). Experimental study of the effect of acute[1] and of chronic[2] mitral insufficiency in dogs has shown that the lesion is well tolerated, provided the insufficiency is not too great. From optical records taken of the pressure changes in the left auricle, left ventricle, aorta, and pulmonary artery in acute mitral insufficiency[1] it was shown that systolic and diastolic aortic pressures fall for two to four beats following the production of insufficiency, resulting in a diminution of the pulse pressure. After a brief period equilibrium was established at a reduced level and the pulse pressure was restored to normal, restoring the normal systolic discharge of the left ventricle. After the lesion was produced, auricular pressure rose and remained elevated at a constant level. It was concluded that the left ventricle quickly compensates for the lesion and thus restores a normal balance of the systolic discharges of the right and left ventricles. Little regurgitation was shown to occur during the isometric period, because of the briefness of this phase, and most of the leak takes place during ejection and in early diastole. As long as the cardiac muscle was efficient, no back pressure effect was felt by the right heart and the pressure in the pulmonary artery remained normal. The duration of the systolic phases was shown to be practically unaltered—once the lesion was stabilized. A very slight lengthening of the isometric period was noted in the first cycle following production of the lesion, the phase returning to normal or lengthening slightly immediately. The variation was never more than a few thousandths of a second. Immediately after insufficiency was produced the ejection period was slightly shortened and then was immediately restored to normal.

Clinical Observations.—Fifteen young patients with clinical evidence of mitral insufficiency were the subjects of this study. The diagnosis of mitral insufficiency was made on the following evidence: (1) history of rheumatic fever; (2) cardiac enlargement; (3) a blowing systolic murmur at the apex which is transmitted to the axilla replacing the first heart

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sound or following it; (4) orthodiagraphic evidence of mitral insufficiency —enlargement of the left ventricle and dilatation of the left auricle. In no instance was there clinical evidence of active infection or of failure, and the blood pressure was within normal limits. The method of study has been given in a previous report.[6] Briefly, the measurements of the phases of the cardiac cycle were made clinically from simultaneous records of the heart sounds and of the subclavian pulse. Lead II of the electrocardiogram was recorded at the same time to check the cardiac mechanism. The heart sounds when recorded at the apex show the systolic and diastolic murmurs well, but the first and second heart sounds were often buried and could not be accurately used for purposes of measurement. When the stethoscopic attachment is moved away from the apex toward the midline the sounds are accurately recognized. In Table I the results of the average measurements of the phases of the cardiac systole are given. The previous diastole was measured in all instances. The cardiac mechanism was normal and was checked electrocardiographically. The isometric period varied from 0.017 to 0.065 sec. (average 0.032 sec.). In one case the lower figure (0.017 sec.) was slightly under the minimum normal as given by Wiggers and Clough[5] and by Katz and Feil.[6] In all other cases this phase was within normal limits but with a tendency to be nearer the lower figure.

The average ejection phase was normal, varying from 0.189 to 0.255 sec. Total systole (Col. 5) may be compared with the calculated systole ($S = 0.31 \sqrt{c}$, Col. 6). In all instances the calculated S exceeds ejection by 0.007 to 0.043 sec. (averaging 0.025 sec.) which is the usual difference in normal persons and represents protodiastole.

Summary.—Total systole and the chief phases of systole (isometric and ejection periods) were measured in fifteen patients with clinical evidence of mitral insufficiency of rheumatic origin. In all instances total systole

TABLE I
MITRAL INSUFFICIENCY

CASE	HEART RATE	ISOMETRIC PERIOD	EJECTION PERIOD	TOTAL SYSTOLE	CALCULATED SYSTOLE ($S = .31 \sqrt{c}$)	CALCULATED SYSTOLE MINUS EJECTION
J. M.	78	0.030 sec.	0.255 sec.	0.285 sec.	0.271 sec.	0.016 sec.
C. R.	78	0.031	0.232	0.263	0.270	0.038
P. V.	81	0.034	0.242	0.276	0.266	0.024
P. G.	86	0.048	0.237	0.285	0.258	0.021
A. S.	87	0.026	0.227	0.253	0.257	0.030
A. L.	88	0.027	0.232	0.259	0.255	0.023
M. H.	89	0.024	0.245	0.269	0.257	0.012
A. K.	90	0.040	0.208	0.248	0.251	0.043
D. S.	94	0.065	0.228	0.293	0.245	0.017
A. K.	95	0.047	0.208	0.255	0.246	0.038
T. J.	100	0.023	0.219	0.242	0.239	0.020
M. B.	104	0.033	0.201	0.234	0.235	0.034
C. B.	105	0.021	0.222	0.243	0.234	0.012
J. D.	109	0.018	0.189	0.207	0.230	0.041
R. S.	116	0.017	0.215	0.232	0.222	0.007

and the phases of systole were found to be within normal limits. When measured systole is compared with calculated systole, the normal difference is found to be present. These measurements are in agreement with experimental studies in this lesion as produced acutely by Wiggers and Feil.[1]

MITRAL STENOSIS

This valve lesion has been produced experimentally by a number of investigators. Katz and Siegel[3] studied the effects of acutely produced stenosis, and Powers, Pilcher and Bowie[4] studied the effect of chronic stenosis. The various methods of production of the experimental lesion and the study of the dynamics have been reviewed by the latter authors. The results of the various experimental workers have varied. Those of Katz and Siegel who produced acute stenosis of the mitral valve confirmed the work of some of the earlier investigators. They found that the heart rate was slowed in some instances. Total systole, and with it ejection of both ventricles, was abbreviated equally in most of the experiments. Therefore it was concluded that this change was not due directly to the valve lesion but rather was due to the diminution in coronary flow because of the fall in aortic blood pressure. Further, left auricular pressure was elevated and with it an increase in the magnitude of left auricular contraction. The pressure maximum of the left ventricle was decreased, resulting in a fall in systolic, diastolic and pulse pressures in the aorta. Variable pressure effects were noted on the right side. Occasionally presystolic vibrations were seen on the curves recorded from the left ventricle. An increase in rate of filling of the left ventricle occurred as evidenced by the steeper gradient of the left ventricular pressure curve during diastasis. Powers, Pilcher and Bowie[4] made observations on five dogs with experimentally produced chronic mitral stenosis. In four of these animals the cardiac output ranged from 104 c.c. to 230 c.c. per kilogram per minute which figures are within normal limits. The output of the fifth animal was distinctly elevated, being 323 c.c. per kilogram per minute. The basal pulse rate was increased in four instances and normal in the fifth. The blood pressure was elevated in only one case.

Clinical Observations.—Twenty-one patients with conclusive clinical signs of mitral stenosis were the subject of this study. Twelve patients had normal mechanism and nine patients had auricular fibrillation, all confirmed by electrocardiograms. In Table II is seen the duration of the phases of systole together with the heart rates which varied from 61 to 94. Both the isometric and ejection periods were within normal limits (isometric period 0.012 to 0.064 sec.), (ejection period 0.217 to 0.281 sec.). Total systole was normal (from 0.248 to 0.324 sec.). Calculated systole when compared with ejection showed the normal difference (i. e., 0.014 to 0.045 sec.) in all instances but one. This patient, No. 9, had a difference of 0.056 sec. slightly in excess of the others.* It may be concluded therefore

*Patient 9 had signs of early cardiac failure, and this fact was doubtless responsible for the shortening of ejection and of total systole.[7]

TABLE II

MITRAL STENOSIS, NORMAL MECHANISM

CASE NO.	HEART RATE	ISOMETRIC PERIOD	EJECTION PERIOD	TOTAL SYSTOLE	CALCULATED SYSTOLE ($s = .31\sqrt{c}$)	CALCULATED SYSTOLE MINUS EJECTION
5	61	0.043 sec.	0.281 sec.	0.324 sec.	0.305 sec.	0.024 sec.
9	67	0.012	0.236	0.248	0.292	0.056*
8	72	0.038	0.268	0.300	0.282	0.014
1	74	0.045	0.239	0.284	0.284	0.045
7	75	0.064	0.255	0.310	0.277	0.022
4	76	0.025	0.254	0.279	0.275	0.021
10	76	0.032	0.268	0.301	0.275	0.007
2	81	0.026	0.243	0.269	0.268	0.025
12	81	0.067	0.243	0.310	0.268	0.025
6	82	0.047	0.241	0.288	0.265	0.024
11	91	0.039	0.217	0.257	0.251	0.034
3	94	0.028	0.228	0.259	0.247	0.019

*Patient had evidence of greater reduction of cardiac reserve.

TABLE III

MITRAL STENOSIS, AURICULAR FIBRILLATION

CASE NO.	HEART RATE	ISOMETRIC PERIOD	EJECTION PERIOD	TOTAL SYSTOLE	CALCULATED SYSTOLE ($s = .31\sqrt{c}$)	CALCULATED SYSTOLE MINUS EJECTION
15	55	0.069 sec.	0.261 sec.	0.330 sec.	0.322 sec.	0.061 sec.
14	69	0.056	0.198	0.254	0.290	0.092
12	76	0.119	0.190	0.309	0.275	0.085
11	90	0.044	0.200	0.244	0.253	0.053
10	93	0.061	0.181	0.242	0.248	0.067
9	94	0.093	0.173	0.266	0.247	0.074
8	96	0.069	0.182	0.251	0.245	0.063
5	111	0.036	0.194	0.233	0.228	0.034
2	151	0.047	0.128	0.175	0.195	0.067

that in clinical mitral stenosis with normal mechanism no variation occurs in the duration of the chief phases of systole or in total systole. Table III shows the findings in the nine patients who had in addition, auricular fibrillation, but who had no evidence of congestive circulatory failure. The heart rates varied from 55 to 151 and the blood pressure was within normal limits. The isometric period varied from 0.036 to 0.119 sec. with an average of 0.07 sec. and was therefore slightly lengthened. Ejection varied from 0.128 to 0.261 sec. Total systole varied from 0.175 to 0.330 sec. When the calculated systole is compared with ejection, it is noted that the difference between these two figures varied from 0.061 to 0.092 sec. (average 0.062 sec.). This is in excess of the normal difference (0.028 sec.) and represents the shortening of ejection and with it total systole (previously reported in patients with auricular fibrillation).[6] This shortening is due to the lack of the auricular contribution to ventricular filling which results in a reduction in the initial volume and tension of the left ventricle.

DISCUSSION

Clinical mitral insufficiency, as is the case in the experimental acute lesion, does not appreciably alter the duration of the isometric and ejection phases of systole. Likewise total systole falls within normal limits. When the duration of ejection is subtracted from the calculated systole, the normal difference is found (protodiastole). Clinical mitral stenosis, with normal mechanism, likewise did not show any deviation from the normal except in one instance (Case 9) where some degree of failure was present. This isolated abbreviation of systole we attribute to the element of failure. These normal figures are in agreement with the findings in the acute experimental lesion where the slight abbreviation of systole was found to be due to the interference with coronary flow. When mitral stenosis was associated with auricular fibrillation, abbreviation of ejection and of total systole occurred. This we believe was due to the lack of synergic auricular contraction and the absence of the auricular contribution to ventricular filling. We may conclude that stenosis of the mitral valve alone does not alter the dynamics of left ventricular systole. To compensate for the narrowed opening auricular hypertrophy occurs and the initial volume and tension of the left ventricle are not lessened. This is in agreement with pathological findings in this valve lesion—an hypertrophied and dilated left auricle. In the clinic we find little or no reduction in the pulse volume in mitral stenosis unless cardiac failure or auricular fibrillation occurs.

SUMMARY

Patients with mitral valve lesions were studied by means of the Wiggers modification of the Frank capsule and the measurements of the chief phases of systole were compared with the duration of these phases calculated from the formula $S = .31 \sqrt{c}$ from which the following conclusions were drawn:

Mitral Insufficiency.—The duration of the isometric and ejection phases and of total systole were within normal limits with one exception.

Mitral Stenosis.—In eleven of the twelve cases with normal mechanism the phases of systole and of total systole were normal. In one instance with slight failure, ejection and total systole were abbreviated. In nine patients with auricular fibrillation but with no signs of failure the phases of systole and total systole were shortened. These clinical findings are in agreement with recent experimental data.

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HEART DISEASE IN GENERAL MEDICAL PRACTICE*

Preliminary Report of Morbidity Survey Conducted by the New York State Department of Health

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HEART disease is the leading cause of death in this country. In 1929 almost a quarter of a million deaths in the registration area of continental United States were ascribed to diseases of the heart—more than double the mortality from cancer, which was second in numerical importance.

The death rates of the forty-six registration states ranged from a minimum of 90 per 100,000 in Oklahoma to a maximum of 304 in Vermont. A rate below 100 was recorded in one other state—New Mexico, 92; twenty-five states had rates between 100 and 200 and eighteen states between 200 and 300 (Fig. 1).

Various factors are responsible for this great variation in the rates; one, the age composition of the population, is self-evident. Since the death rate from heart disease increases with age, a state with an old population, because of this fact alone, will have a higher death rate than a state with a young population. The weight of the age composition can be easily evaluated numerically—relating the death rates to the proportion of persons in the population who were more than forty-five years of age, we find the coefficient of this correlation to be most significant: $+0.832 \pm 0.031$.

In 1928, the latest year for which the information is available, heart disease was ninth in importance among the causes of death of children between one and ten years of age, pneumonia being first, followed in order by accidents, diarrhea and enteritis, diphtheria, influenza, tuberculosis, measles, and whooping cough. Between ten and fifteen years, heart disease was second, accidents being first. In the age group fifteen to twenty-four years, heart disease was fifth, accidents being first, followed by tuberculosis, pneumonia, and puerperal causes. Heart disease was third in the next age group, twenty-five to thirty-five years, tuberculosis leading, with accidents second. Between thirty-five and forty years, heart disease was second and tuberculosis first. At all ages after the fortieth year, heart disease held first place.

The percentage of deaths ascribed to heart disease in the registration states increased quite uniformly with age, with the exception of a singular peak at ten to fourteen years (Fig. 2). This relatively high mortality was not unique for 1928; the corresponding figures in the preceding years demonstrate the same fact. Between five and forty years, heart disease

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was relatively more important among females than males; in the age groups forty to forty-four years and "seventy-five years and over" the ratios for the sexes were the same, while in the other age groups the percentage was higher among males.

Although most of the deaths from heart disease occur at the farther end of life, the number of deaths in the younger ages is by no means small. In 1928, for example, the deaths of 30,675 persons under forty-five years

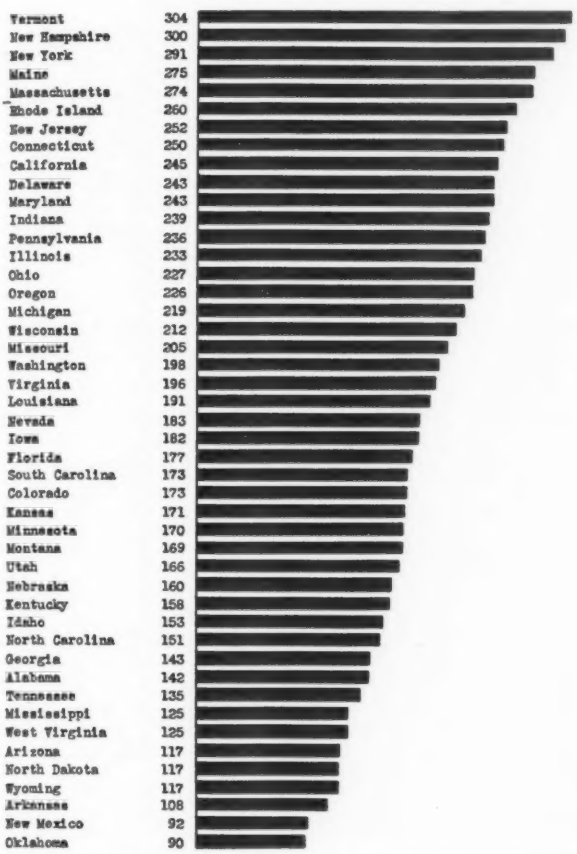

Fig. 1.—Death rates per 100,000 population, from heart disease, registration states, 1929.

of age were recorded in the entire registration area. This is a larger number than the deaths at all ages during that year from many important causes: typhoid fever (5,620), diabetes (21,747), diseases of the puerperal state (15,691).

Mortality From Heart Disease in New York State.—The six leading causes of death in the state of New York in 1930 were: heart disease (277 per 100,000 population); cancer, all forms (123); pneumonia, all forms (102); accidents (81); acute and chronic nephritis (77); and tuberculosis, all forms (71).

In 1900, heart disease, with a rate of 133, was fourth among the causes of death, being preceded by tuberculosis (217), pneumonia (217), and diarrhea and enteritis, all ages (148), (Fig. 3).

In the course of thirty years the death rate from heart disease more

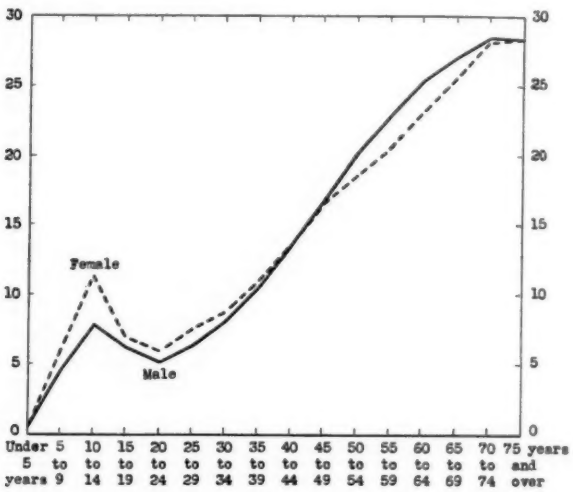

Fig. 2.—Deaths from heart disease per 100 deaths from all causes, by sex and age, registration states, 1928.

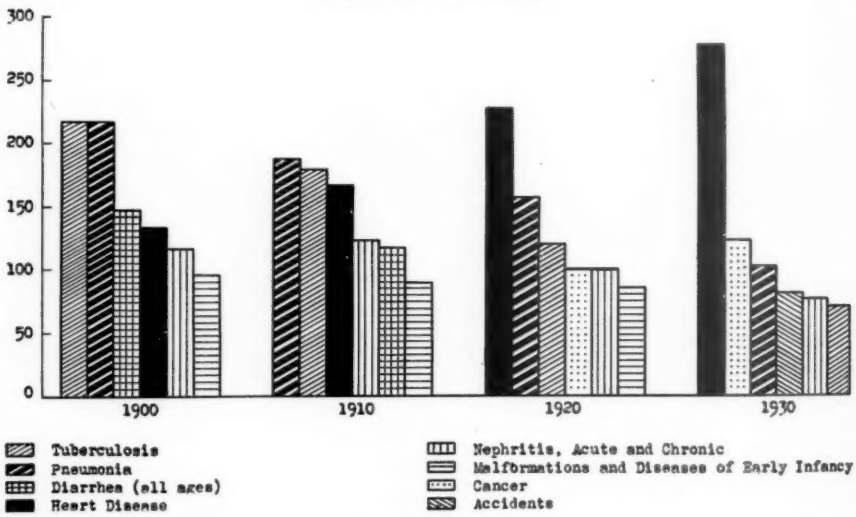

Fig. 3.—Death rates per 100,000 population, from leading causes, New York state, 1900, 1910, 1920, 1930.

than doubled, while mortality from the other causes either rose by a smaller increment (cancer from 67 to 123, or 84 per cent; accidents from 78 to 81) or decreased (Fig. 4).

The mortality from heart disease has been mounting steadily since the beginning of the century with the exception of 1905, 1908, 1919, 1927, and

1930. The recession of the death rate in 1927 may be explained by the fact that the high rate of 1926 was a direct consequence of unusually severe weather in February, March, and April of that year. In 1919, as a sequel to the influenza epidemic, the contingent of sufferers from heart disease was considerably reduced; the drop in the rate in 1905, 1908, and 1930 similarly followed the uncommon prevalence of influenza and pneumonia in the immediately preceding years: 1904, 1907, and 1929. The death rate from heart disease in the latter year was the highest ever recorded in the state—the January rate (421.7) establishing the present maximum for any month. The direct bearing of influenza and respiratory diseases on the mortality from heart disease was demonstrated by an analysis of the death certificates for the state, outside of New York City, for January, 1929. Of the 2,345 deaths attributed to heart disease as a primary cause, 247 were complicated with influenza, 179 with broncho-

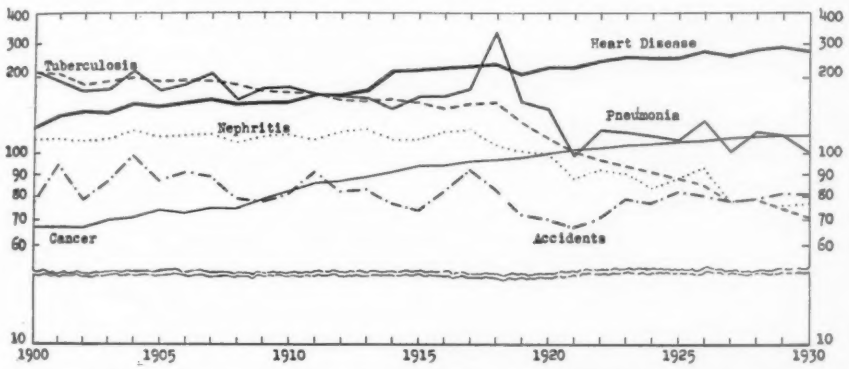

Fig. 4.—Death rates per 100,000 population, from heart disease and other important causes, New York state, 1900-1930.

pneumonia, and 265 with other respiratory diseases—a total of 691 with influenza and other respiratory complications; in January, 1928, the corresponding number was 190. The excess of 501 represents almost two-thirds of the difference in the January deaths in these two years.

Plan and Scope of Heart Survey.—Quantitative studies carried out in recent years indicate that from 2 to 4 per cent of the people are afflicted with heart disease. A survey of sickness[1] was conducted by the New York State Department of Health in 1927, in which more than one hundred physicians, serving a population of one hundred thousand, reported each week cases of various types of disease in their practice. Cases of heart disease totalled 4,123—a larger number than of all reportable communicable diseases, 3,212. In a more intensive survey of a single county, Essex,[2] cases of heart disease totalled 535, while the entire reportable group was represented by only 312 cases.

The next step is, of course, from the general to the particular—from an evaluation of the size of the problem to a study of details. The state-

ment that from four to eight million people in this country, including a large number of children and young adults, suffer from heart disease, is naturally followed by the query: What is to be done about it? Experts tell us that "from the point of view of prevention and relief" it is essential to realize the complex nature of heart disease and here "from practically every point of view, information is inadequate."[3]

Certain clinics and hospitals have done a great deal of good work in an-

SURVEY OF MORBIDITY FROM DISEASES OF THE HEART

Confidential report by.....M. D. Date.....
.....P. O.

Name of patient.....Age.....Sex.....Color.....
Single.....Married.....Widowed.....Divorced.....Country of birth.....Occupation.....
Have others in family heart disease? Yes.....No.....Unknown.....If so, what was their age when disease was discovered.....

Etiology

1 Rheumatic fever.....
Date of first attack.....
2 Chorea.....
3 Syphilis.....
Date of chancre.....
4 Other infection (specify organism).....
State nature of infection (diphtheria, etc.).....
.....
5 Congenital.....
6 Chronic high blood pressure.....
7 Thyrotoxicosis.....
8 Other causes (specify).....
.....
9 Etiology unknown.....
10 Nervous heart.....

Pathology

1 Pericardial disease: (a) Inflammation..... (b) Effusion.....
2 Damage to valves, state valve affected.....
3 Aortitis..... Aneurism.....
4 Damage to coronary vessels.....
5 Damage to myocardium.....

Course of patient's disability

State date or age of patient at beginning of:
(a) Cardiac symptoms.....
(b) Occasional rest in bed.....
(c) When patient first became bedridden.....
(d) When patient became permanently bedridden.....

Type of treatment

1 Removal of foci of infection: (a) Tonsillectomy..... (b) Other foci (specify).....
2 Anti-luetic treatment.....
3 For hypertension.....
4 Cardiac treatment: (a) By drugs..... (b) By rest.....
5 Other treatment.....

Remarks: (Use reverse side if necessary)

Fig. 5.

alyzing and making public their experiences with cardiac patients, but here it is the more advanced stages of heart disease that are dealt with. It is the general practitioner who sees the early symptoms; his observations are certainly as worthy of study and may produce as valuable results as the more detached conclusions of specialists. Since cases of heart disease are not reportable, facts from private practice can be collected only with the voluntary cooperation of physicians. That such cooperation may be secured was demonstrated by the two surveys of general morbidity

mentioned earlier. A proposal for a survey of morbidity from heart disease to be conducted by the New York State Department of Health, outlined before the American Heart Association, received the endorsement of the Association as well as of the State Medical Society.[4]

The survey commenced in January, 1931, and during the first six months of the year reports were received from 186 physicians practicing in urban and 110 in rural communities—a total of 296.

The purpose of the general questions in the report form (Fig. 5), as well as those relating to etiology, pathology, and type of treatment, needs no elaboration. The section relating to the course of the patient's disability was inserted with the hope that if the answers are sufficiently numerous and complete it may be possible to make a mathematical determination of the important stages in the life of a cardiac patient.

GENERAL RESULTS

This paper will be limited to a provisional anlysis of the 1,934 cases reported in January to June, 1931. No reference will be made to the course of the patient's disability or to the type of treatment employed. It is hoped to discuss these facts, as well as details of the other items, in a subsequent study.

Sex and Conjugal Condition.—The distribution of the cardiac cases according to the sex and conjugal condition of patient is shown in Table I.

TABLE I

MARITAL CONDITION	TOTAL	MALE	FEMALE
Total	1,934	933	1,001
Single	453	227	226
Married	1,062	555	507
Widowed	362	125	237
Divorced	15	4	11
Unknown or not stated	42	22	20

There is no special significance in the excess of married men and widowed women; this is very likely a reflection of the relative size of these classes in the general population. According to the census of 1930, there were in the State of New York 2,761,908 married men and 2,738,973 married women.* Similarly, the number of widows, 522,983, was more than double the number of widowers, 197,157.

Color and Nativity.—The majority of the 1,934 patients were white, the colored numbering only 27 (negroes, 22; other colored, 5). Among the white, the number of native-born (1,504) was six times that of the foreign-born (255).

*This apparent paradox undoubtedly results from the fact that at the time the census was taken the wives of a number of foreign-born men resided abroad.

TABLE II

COLOR AND NATIVITY	TOTAL	MALE	FEMALE
Total	1,934	933	1,001
White	1,907	919	988
United States	1,504	719	785
Total foreign	255	131	124
Austria	3	2	1
Canada	29	18	11
Denmark, Norway, Sweden	7	3	4
England, Scotland, Wales	25	14	11
Germany	39	18	21
Hungary	2	–	2
Ireland	32	17	15
Italy	48	22	26
Poland	46	25	21
Russia	11	5	6
Other foreign countries	13	7	6
Country not stated	148	69	79
Colored	27	14	13
Negro	22	10	12
Other colored	5	4	1

Occupation.—Of the 933 males, the occupation of 43 was not stated; of the remainder, 90 were under twenty years, practically all of whom had no stated occupation. The percentage distribution of the remaining 800 over twenty years of age was as follows:

Total	100.0
No occupation	19.6
Farmers	13.4
Unskilled laborers	11.0
Skilled laborers	10.0
Merchants, retail dealers, "business men"	7.0
Clergymen, physicians, lawyers, teachers, members of other professions	6.1
Clerical workers	6.1
Factory operators	4.3
Salesmen, including retail clerks	2.5
Chauffeurs, truck drivers, delivery men	2.0
Railroad workers	1.9
Insurance and real estate agents	1.7
Caretakers, watchmen, janitors	1.6
Gardeners	1.3
Factory owners, managers, officials	1.3
Foremen	1.3
Other occupations	8.9

The occupation of 28 of the 1,001 females was not stated. Deducting those under twenty years, practically all of whom had no stated occupation, we have 868, regarding whose occupation some definite statement was entered. The percentage distribution by occupation was as follows:

Total	100.0
No occupation	12.8
Housewives	70.2
Teachers	3.0
Clerical workers	2.9
Nurses	2.9
Domestic and personal service	2.8
Factory operators	1.0
Other occupations	4.4

Most of the persons without occupation were over sixty years: 103 of the 157 males and 84 of the 109 females.

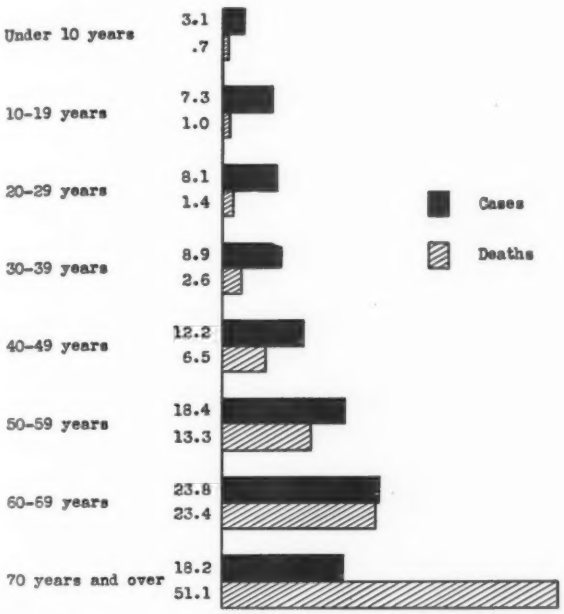

Fig. 6.—Percentage distribution by age of patients in heart survey and of deaths from heart disease in upstate New York, 1930.

Age.—In Table III is shown the distribution of 926 males and 992 females according to age (the ages of 7 male and 9 female patients were not given); and in Fig. 6 the percentage distribution of all deaths from heart disease in upstate New York in 1930.

The curves of cases for both males and females have a low point in the youngest age group, rising to a maximum at sixty to sixty-nine years and declining in the oldest group "seventy years and over."

The percentages of morbidity and mortality are strikingly different except in the age group sixty to sixty-nine years in which they are practically the same: 26.0 per cent of the males being in this group, in which occurred 25.1 per cent of the deaths; among the females, the corresponding percentages are 22.1 and 21.4. Under forty years is found one-quarter of all male cases as compared with 5.5 per cent of the deaths; among

females, 29.9 per cent of the cases and 5.8 per cent of the deaths. In the oldest group "seventy years and over" fall one-fifth of the patients and almost one-half, 47.4, of the total male deaths; among females, 16.8 per cent of the cases and 55.3 per cent of the deaths.

TABLE III

AGE	TOTAL		MALE		FEMALE	
	CASES	DEATHS	CASES	DEATHS	CASES	DEATHS
Total	100.0	100.0	100.0	100.0	100.0	100.0
Under 10 years	3.2	0.7	3.1	0.7	3.3	0.6
10-19 years	7.2	1.0	7.1	1.0	7.3	1.1
20-29 years	8.1	1.4	7.0	1.3	9.1	1.5
30-39 years	8.9	2.6	7.5	2.5	10.2	2.6
40-49 years	12.0	6.5	9.8	7.2	14.1	5.8
50-59 years	18.5	13.3	20.0	14.8	17.1	11.7
60-69 years	24.0	23.4	26.0	25.1	22.1	21.4
70 years and over	18.1	51.1	19.5	47.4	16.8	55.3
Average age	51.5	67.6	52.9	66.7	50.3	68.7
Median age	55.7	70.3	57.7	69.0	53.5	71.7

The average age of all patients was 51.5 years; males, 52.9 and females, 50.3; the corresponding median ages were 55.7, 57.7, and 53.5. The average ages at death from heart disease in 1930 were 67.6 for both sexes, 66.7 for males and 68.7 for females; the corresponding median ages were: 70.3, 69.0, and 71.7.

ETIOLOGY

The etiology was indicated in practically all of the reports; the distribution of the important types by sex is shown in Table IV.

TABLE IV

ETIOLOGY	NUMBER			PER CENT		
	TOTAL	MALE	FEMALE	TOTAL	MALE	FEMALE
Total	1,872	907	965	100.0	100.0	100.0
Congenital	45	23	22	2.4	2.5	2.3
Rheumatic infections	511	221	290	27.2	24.3	30.0
Syphilis	86	65	21	4.6	7.2	2.2
Other acute infections	272	127	145	14.5	14.0	15.0
Arteriosclerosis	164	90	74	8.8	9.9	7.7
Hypertension	376	161	215	20.1	17.8	22.3
Thyrotoxicosis	67	11	56	3.6	1.2	5.8
Other factors	134	74	60	7.2	8.2	6.2
Unknown	217	135	82	11.6	14.9	8.5

N. B. Rheumatic infections comprise: rheumatic fever, 409; tonsillitis, 75; chorea, 27; other infections: streptococcus (mainly scarlet fever), 57; teeth, 43; influenza, 42; pneumonia, 32; diphtheria, 23; typhoid fever, 14; unclassified, 61.

In 27.2 per cent of the cases, rheumatic infection was given as the etiological factor. Hypertension was next, 20.1 per cent; other acute infections, 14.5 per cent; arteriosclerosis, 8.8 per cent; syphilis, 4.6 per cent; thyrotoxicosis, 3.6 per cent; congenital, 2.4 per cent. The etiology of 11.6 per cent of the cases was unknown (Fig. 7).

The proportion of syphilitic heart disease among males was more than three times that among females, and there was also a greater prevalence, though not to the same degree, of the arteriosclerotic heart. Rheumatic heart was more prevalent among women.

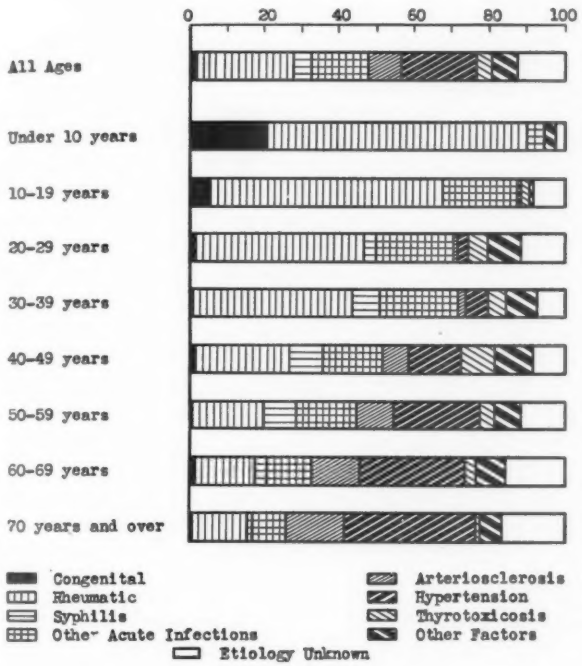

Fig. 7.—Percentage distribution of cases in heart survey by age and etiology.

The leading etiological factor under twenty years was rheumatic infection, 64 per cent; other acute infections being second, 15 per cent; and congenital third, 10 per cent. Rheumatic infection held first place in the next age group twenty to forty years, 44 per cent; followed by other acute infections, 21 per cent; and etiology unknown, 9 per cent. At forty to sixty years, arteriosclerosis combined with hypertension was in first place, 28 per cent; rheumatic infection second, 21 per cent; and other infections third, 16 per cent. After the sixtieth year, arteriosclerosis and hypertension were indicated in 46 per cent; rheumatic infection in 16; and unknown etiology in 15 per cent. Age forty years is frequently taken as a dividing line for the leading etiological types of heart disease. Their

percentage distribution under forty and over forty, as well as the median ages, are shown in Table V.

TABLE V

ETIOLOGY	UNDER 40 YEARS	OVER 40 YEARS	MEDIAN AGE
Total	27.4	72.6	55.7
Congenital	55.6	44.4	30.0
Rheumatic infections	52.1	47.9	38.6
Syphilis	20.0	80.0	51.6
Other acute infections	35.8	64.2	51.8
Arteriosclerosis	3.1	96.9	65.0
Hypertension	4.0	96.0	64.8
Thyrotoxicosis	27.3	72.7	47.1
Other factors	22.6	77.4	55.6
Unknown	18.1	81.9	62.0

Cases of rheumatic heart were only slightly more numerous among the younger patients. Syphilitic heart was four times more prevalent after forty years, while practically all cases of arteriosclerosis and hypertension fell in the older group. Cases of unknown etiology, contrary to the findings in some clinical studies, were largely represented in the older group.

PATHOLOGY

A definite statement of pathological changes was made in 1,826 cases. The distribution according to sex is shown in Table VI.

Damage to valves represented about one-half of the specified types; the proportion being markedly greater in females than males. In practically

TABLE VI

PATHOLOGY	NUMBER			PER CENT		
	TOTAL	MALE	FEMALE	TOTAL	MALE	FEMALE
Total	1,826	893	933	100.0	100.0	100.0
Damage to valves	888	402	486	48.7	45.0	52.1
Mitral	693	306	387			
Aortic	51	24	27			
Tricuspid	6	3	3			
Mitral and aortic	96	52	44			
Mitral and tricuspid	4	3	1			
All valves	14	7	7			
Valve not stated	24	7	17			
Damage to myocardium	528	248	280	28.9	27.8	30.0
Damage to coronary vessels	361	212	149	19.8	23.7	16.0
Aortitis	28	14	14	1.5	1.6	1.5
Aneurysm	13	10	3	0.7	1.1	0.3
Pericarditis	8	7	1	0.4	0.8	0.1

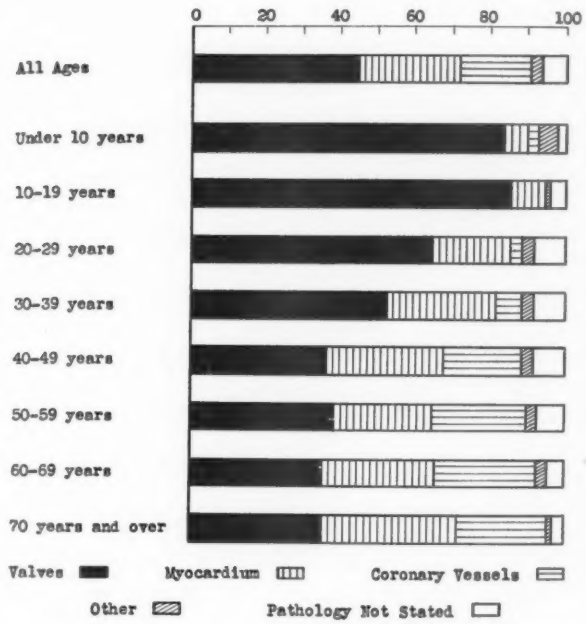

Fig. 8.—Percentage distribution of cases in heart survey by age and pathology.

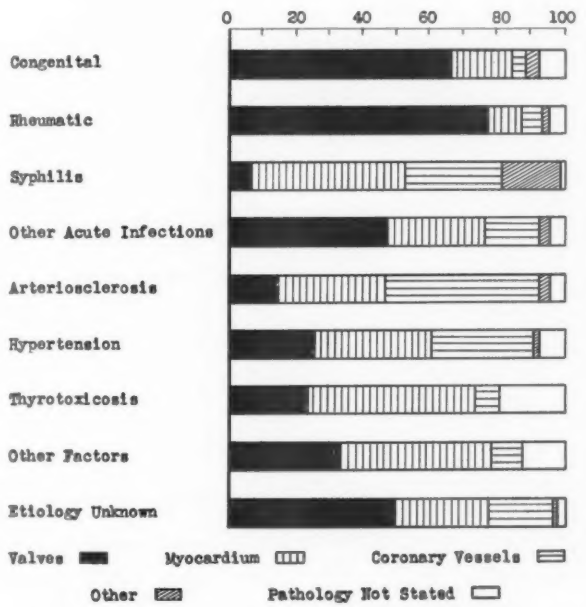

Fig. 9.—Percentage distribution of cases in heart survey by etiology and pathology.

all, the mitral valve was involved, either alone or in combination with others.

The prevalence of valvular defects was inversely related to age. Of the 193 patients under twenty years, 171, or 88.6 per cent, were said to have valvular disease. In the next age group, twenty to forty years, the percentage was 63.9 and after the fortieth year, 39.5. On the other hand, damage to the myocardium and coronary vessels increased with age. The former was present in only 8.3 per cent of the cardiac defects of the patients under twenty years, 27.4 per cent at twenty to forty years, and 30.2 per cent after forty years; the latter, in only 1 per cent of those under twenty years, 5.4 per cent in those twenty to forty years, and 25.7 per cent after forty years (Fig. 8).

The percentage distribution of the three important types of pathological changes among patients under forty and over forty years and the median ages for each type are shown in Table VII.

TABLE VII

PATHOLOGY	UNDER 40 YEARS	OVER 40 YEARS	MEDIAN AGE
Total	27.4	72.6	55.7
Damage to valves	40.9	59.1	49.2
Damage to myocardium	18.8	81.2	60.2
Damage to coronary vessels	5.1	94.9	62.1

Table VIII shows the percentage distribution of the leading etiological types according to pathology. Damage to valves was the major pathological change in congenital heart conditions, also where the etiology was said to be rheumatic infection, "other acute infection" or unknown. Damage to the myocardium was indicated in one-half of the cases with

TABLE VIII

ETIOLOGY	PATHOLOGY					
	TOTAL	DAMAGE TO VALVES	DAMAGE TO MYOCARDIUM	DAMAGE TO CORONARY VESSELS	OTHER	NOT STATED
Congenital	100	67	18	4	4	7
Rheumatic infections	100	78	10	6	2	4
Syphilis	100	7	46	29	17	1
Other acute infections	100	48	29	16	3	4
Arteriosclerosis	100	15	32	46	3	4
Hypertension	100	26	35	30	2	7
Thyrotoxicosis	100	24	50	7	–	19
Other factors	100	34	45	9	–	12
Unknown	100	50	28	19	1	2

thyrotoxicosis as the etiological factor and almost an equal proportion of the syphilitic cases. Damage to the coronary vessels was of prime importance in the arteriosclerotic and only of lesser importance in the hypertensive type (Fig. 9).

SUMMARY

In January, 1931, the New York State Department of Health commenced a survey of morbidity from heart disease in the state, exclusive of New York City.

During the first half of the year 296 physicians reported 1,934 cases: 933 males and 1,001 females.

Age.—The distribution of the patients by age was as follows: under 40 years, 27.4 per cent; between 40 and 60 years, 30.5; 60 years and over, 42.1. The average age was 51.5 and the median age, 55.7 years.

The males were, as a group, younger than the females. Of the former, 24.7 per cent were under 40 years; of the latter, 29.9 per cent. The average age of the males was 52.9 years, the median age, 57.7; the average age of the females, 50.3 years and the median age, 53.5.

Etiology.—The leading etiological factors were: rheumatic infection, 27.2 per cent; hypertension, 20.1; arteriosclerosis, 8.8; syphilis, 4.6; congenital, 2.4; and in 11.6 per cent the etiology was unknown.

The proportion of syphilitic heart disease among males was three times that among females.

Pathology.—Damage to valves was indicated in 48.7 per cent; damage to myocardium, 28.9; to coronary vessels, 19.8.

Coronary disease was more prevalent among males, while valvular disease and damage to myocardium were more prevalent among females. The proportions were: coronary disease—males 23.7 per cent, females 16.0; valvular disease—males 45.0, females 52.1; damage to myocardium—males 27.8, females 30.0.

It is a pleasure to express my thanks to the physicians whose altruistic cooperation made this study possible. I am under obligation to Dr. Robert H. Halsey of New York City for valuable counsel at all stages of the survey. The report form was drawn up with the kind advice of Drs. A. E. Cohn, J. Hamilton Crawford, Herman O. Mosenthal, New York City; Richard C. Cabot and Paul D. White, Boston. For painstaking preparation of the raw material for statistical analysis, I am especially indebted to Miss Elizabeth Parkhurst, Research Statistician of the New York State Department of Health.

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REVERSAL IN DIRECTION OF THE QRS COMPLEX OF EXPERIMENTAL RIGHT BUNDLE-BRANCH BLOCK WITH CHANGE IN THE HEART'S POSITION*†

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IN A previous report[1] we have shown that the electrocardiographic appearance of ventricular extrasystoles elicited experimentally from fixed points is modified by the position of the heart. Rotation of the heart on its own long axis had the most marked influence. In fact, a change in the heart's position often reversed the direction of the QRS complex of the extrasystole in one or more leads. It was concluded from this study that the localization of the origin of the ventricular extrasystoles on the basis of the direction of QRS in Leads I and III was hazardous, especially in abnormal hearts. It was inferred by analogy that it was unsafe to attempt to locate the site of bundle-branch block from the direction of QRS in the various leads. In the present research an attempt has been made to verify this inference with experimental bundle-branch block by determining the influence on the electrocardiogram of shifting the heart's position. This has been carried out successfully in four animals, in three of which the shift to successive positions was performed twice.

PROCEDURE

Each dog, anesthetized with barbital, had chest open and artificial respiration. The right bundle was cut in the intraventricular septum close to the A-V junction with a sharp knife thrust through the right ventricular wall, the procedure being essentially like the method most recently described by Roberts, et al.[2] The success of the cut in producing bundle-branch block was decided by the change in the electrocardiogram following the cut. A decided change in contour of the record with prolongation of QRS duration was taken to show the presence of block. This was verified postmortem by the location of the cut. Once the block was produced, the position of the heart was altered in the same manner and in the same order as in our extrasystole experiments (see previous report[1]). An electrocardiogram was taken with the ordinary leads in each position of the heart, and at the end of each series with the heart placed in its original position to determine what change in configuration, if any, had developed.

*From the Cardiovascular Laboratory, Department of Physiology, Michael Reese Hospital and the University of Chicago.
†Aided by the Emil and Fanny Wedeles Fund for the study of diseases of the heart and circulation.

RESULTS

No attempt was made to quantitate the change in the electrical axis in the plane of the leads. A complete set of curves of one series of positions in Experiment A 12 is shown in Figs. 1 and 2.

The four segments of Fig. 1 show the change in appearance of the electrocardiogram as the heart's apex was elevated on the transverse axis at the base. The most noticeable change to be seen is the increase in

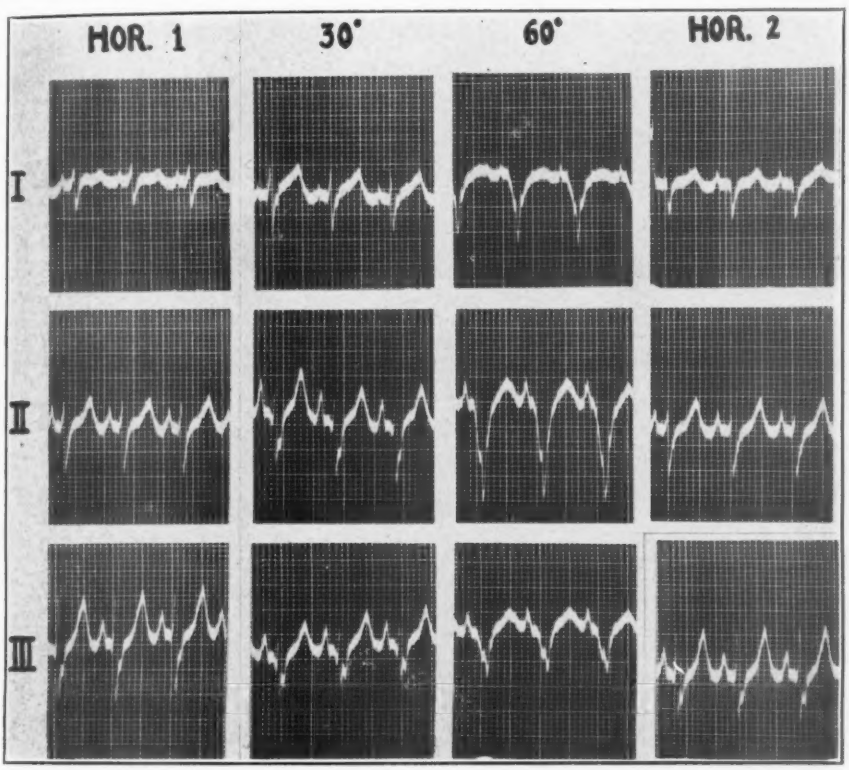

Fig. 1.

Figs. 1 and 2.—Segments of the three leads of the electrocardiograms taken in one of the two series of positions of Dog A12. The positions of the heart are: Hor. 1, heart horizontal and apex pointing caudad at start of series of positions; 30° and 60°, heart up to form, respectively, an angle of 30° and 60° with the long axis of the body, heart's apex pointing caudad; Hor. 2, position similar to Hor. 1, taken at end of series; RVA, heart's apex up 30°, to the right 15° of the long axis of the body, and heart rotated on its own long axis to bring right ventricle more anteriorly. LVA, heart's apex up 30°, to the left 15° of the long axis of the body, and heart rotated on its own long axis to bring the left ventricle more anteriorly. Note complete reversal of QRS_1 and QRS_3 in last two positions.

duration of the QRS straddle as the heart's apex points more and more anteriorly (compare Hor. 1, 30° and 60° of Fig. 1). The fourth segment of Fig. 1 (Hor. 2) shows the appearance of the electrocardiogram when the heart is returned to its original position after being placed in the whole series of positions shown in the other seven segments of Figs. 1

and 2. The electrocardiogram at the end is essentially the same as that taken at the start with the heart in this position (compare Hor. 1 and Hor. 2 of Fig. 1). This constancy of the electrocardiogram in the same position excludes the possibility that the changes in other positions of the heart might be due to an alteration in the character of the block. Any modifications that do occur therefore must be ascribed to the altered position of the heart. A similar check occurred in the other two animals

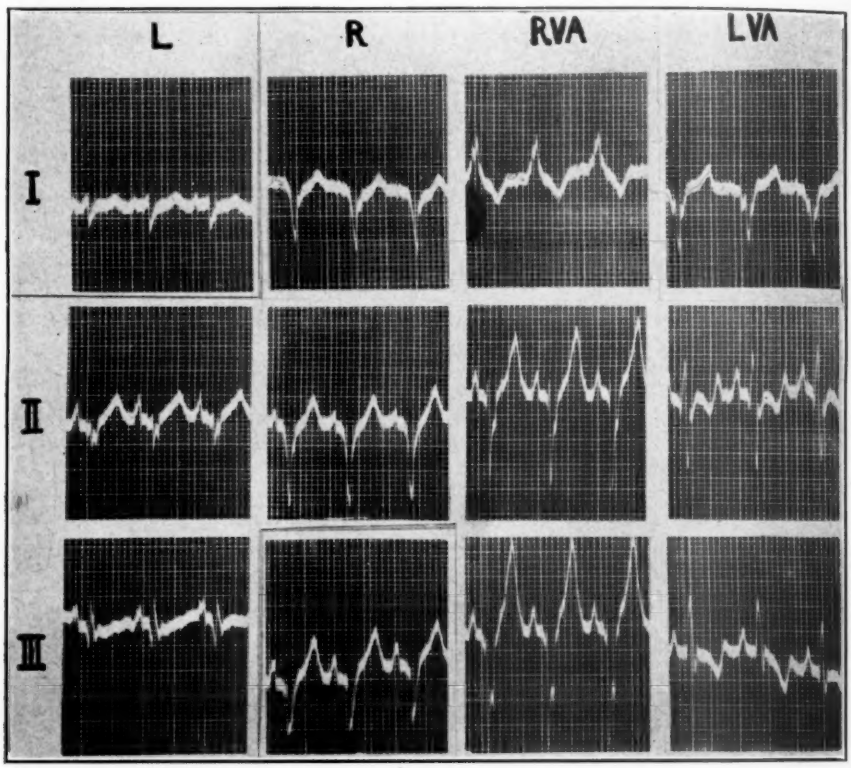

Fig. 2.—See legend under Fig. 1.

in which a curve was taken when the heart had returned to its original position.

It was found that the electrocardiographic deflections of the bundle-branch block were smaller when the heart's apex was to the left of the long axis of the body, without rotation of the heart on its own long axis, than when the apex was to the right of the long axis of the body. In three of the seven experiments the direction of QRS was reversed in Lead III when the heart was moved from one to the other position, viz., the inverted QRS in Lead III became upright on the shift from right to left. Fig. 1 shows a change in Lead III which is a step toward reversal. In one experiment a similar tendency occurred in Lead I in a reverse direction.

Without fail in the seven experiments, a complete reversal of QRS in Leads I or III was obtained when the heart was rotated on its own long axis from a position where the right ventricle was more anterior than normal to one where the left ventricle was more anterior than normal. The angle of rotation between the two positions was about 50°. In three of the experiments a reversal occurred in both Leads I and III, viz., in Figs. 2 and 3 (compare RVA and LVA) it will be seen that the QRS which was up in Lead I and down in Lead III in the first of these positions (RVA), became inverted in Lead I and up in Lead III in the other (LVA).

DISCUSSION

According to the classical viewpoint the curve shown in segment RVA of Figs. 2 and 3 would be classed as a right bundle-branch block, and the curve shown in segment LVA of Figs. 2 and 3 as left bundle-branch block; the terminology introduced by Wilson[3] would reverse the location. Yet the lesion in the heart was constant and was located in the right bundle-branch, as shown (1) by postmortem check, (2) by the return of the electrocardiogram to its first contour when the heart was restored to its original position, and (3) by the ability to repeat the same sequence of change twice in each of three animals. It appears proved from these experiments that the position of the heart does modify the electrocardiogram of bundle-branch block and can simultaneously completely reverse the direction of QRS in Leads I and III.

These experiments lend support to the contention presented in our previous communication,[1] viz.: "In the present state of knowledge and with the variability in direction of the QRS group which these experiments show can be produced by changing the position of the heart, it would be preferable not to attempt to locate the site of origin of ventricular extrasystoles and, for the same reason, bundle-branch block."

Furthermore, the argument that autopsy and electrocardiographic evidence do not correspond if the latter is interpreted according to the classical terminology, but do correspond if the Wilson terminology[3] is applied, is not borne out when the data is critically examined. Mahaim[4] has recently shown in an excellently carried out study and critique of reported observation that there is agreement in the majority of cases of his own series and those reported between the anatomical and electrocardiographic diagnosis when the latter is interpreted according to the classical terminology. He criticizes some of the earlier studies on the ground that the histological examinations were incomplete. Exceptions do occur, however, and, from our experiments, can be explained by alterations in the configuration of the heart due to position changes or preponderant hypertrophy of the ventricles. Such changes in the heart's configuration can be as great clinically as those produced in these experiments. This is evidenced by the marked alteration in the electrical axis in the plane of the leads encountered especially in left ventricu-

lar preponderant hypertrophy in which QRS is inverted in Leads II and III.

The contention presented here that the position of the heart modifies the electrocardiographic appearance of bundle-branch block is significant regardless of whether the classical or Wilson's interpretation of bundle-branch block is finally accepted as correct. Our results offer an explanation which will account for those apparent discrepancies between autopsy and electrocardiographic interpretations of bundle-branch block. It will

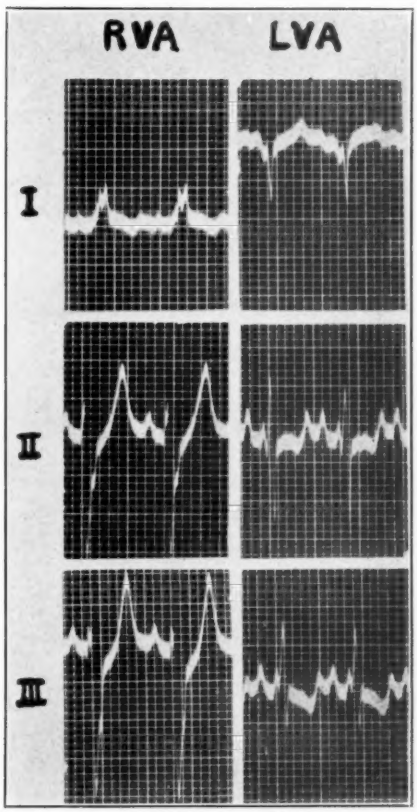

Fig. 3.—Segments of the three leads of the electrocardiograms taken in two positions of heart of Dog A13 to illustrate the complete reversal of QRS_1 and QRS_3 as in Fig. 2. RVA and LVA as in Fig. 2.

also avoid the difficulty of changing the interpretation from left ventricular preponderance to right bundle-branch block in cases such as we have seen and those reported by Luten[5] and by Morris and McGuire,[6] where the QRS complex, inverted in Leads II and III and of normal duration in a series of curves, shows a progressive increase in its duration beyond normal limits, or where a seeming right bundle-branch block would be called left ventricular preponderance when the abnormally long duration of QRS decreases to within normal limits. As stated previously by

one of us,[7] it is more likely that when marked preponderance is present the bundle-branch block increases the duration of the QRS, and the preponderant hypertrophy determines the direction of the major initial deflection in the three leads.

We therefore advocate that no attempt be made in man to localize the bundle involved from the appearance of the electrocardiogram. Instead the diagnosis should be given as follows: 1, intraventricular block of the so-called bundle-branch block type, and 2, left (or right) axis deviation (or preponderant hypertrophy).

SUMMARY

It can be demonstrated that the contour of experimentally produced right bundle-branch block is modified by changing the heart's position. The direction of QRS can be reversed in Leads I or III, or in both, by moving the heart's apex from left to right of the body's long axis, especially when the heart is at the same time rotated on its own long axis. This shift alone may change a seeming right to a seeming left bundle-branch block or vice versa, depending on whether the classical or Wilson's terminology is used, as is shown in the illustrations of this report. This last observation explains the apparent discrepancies between the electrocardiographic and the autopsy diagnosis of the branch involved in bundle-branch block.

It is recommended that no attempt be made to designate the bundle-branch involved; instead in man all such cases should be called intraventricular block of the bundle-branch type.

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A STUDY OF VISCEROCARDIAC REFLEXES*†

I. The Experimental Production of Cardiac Irregularities by Visceral Stimulation

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THE clinical literature presents numerous cases in which an apparent correlation between visceral excitation or disease and cardiac irregularities existed. That such a correlation actually exists in man is definitely supported by the observations of Babcock,[1] Mayo,[2] and Straus and Hamburger[3] who have reported cases of cardiac disorders that improved after biliary tract surgery.

Lennox, Graves and Levine[4] in a study of forty-eight patients during surgical operation, as well as Marvin and his associates[5, 6] in a similar study of sixty patients do not report any changes in the electrocardiogram which could be attributed to manipulation of the viscera.

Recently Ressinger,[7] using needle electrodes, studied a few cases during abdominal and thoracic operations. In a case of cholecystectomy he observed that pulling on the liver caused a slowing of the heart rate and a disappearance of the P-wave. When the stimuli ceased, the heart became normal. In another case of carcinoma of the esophagus, a slight pull on the cardia caused an auricular flutter which went over into a fibrillation. The various waves of the electrocardiogram were markedly "splintered."

Experimentally it is established that cardiac inhibition or acceleration may be induced by visceral excitation. In the frog, tapping or stimulation of the viscera[8, 9, 10] or incision of the gall bladder with a spillage of bile into the upper peritoneal cavity[11, 12] causes reflex inhibition of the heart. In the turtle the same type of stimulation causes acceleration of the heart.[9] In the dog, distention of the gall bladder may cause either an inhibition or an acceleration of the heart rate.[12, 13] In nausea and vomiting, inhibition followed by acceleration is known to occur quite uniformly.[14] Prolonged distention of the stomach causes acceleration of the heart in the dog; and in one out of twelve dogs studied by Burgess, Scott and Ivy,[15] it caused the occurrence of rhythmically recurring ectopic beats. Pearcy and Howard[16] observed occasionally premature contractions in dogs on distention of various viscera after poisoning the heart with barium chloride and found that the sympathetic pathway was concerned. This observation falls in line with the observations of

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Rothberger and Winterberg[17] who were able to produce extrasystoles by sympathetic stimulation after small doses of barium chloride.

In view of the physiological and clinical importance of viscerocardiac reflexes and the rather meager experimental literature on the subject, Dr. A. C. Ivy pointed out that further experimental study of the subject was definitely indicated.

Experimental

Attempts to produce extrasystoles. Part I

The Occurrence of Spontaneous Extrasystoles in the Dog.—As a rule in the anesthetized animals the blood pressure record was observed for cardiac irregularities and then on observing irregularities, the animal was connected to the leads of the electrocardiograph. In experimental work of this nature it is necessary to establish a norm or control series or to ascertain the incidence of spontaneous cardiac irregularities under the experimental conditions to be employed.

For this purpose a "control group" of ninety-five barbitalized dogs was used to determine the incidence of extrasystoles in an experiment in which the operative procedure was quite constant. This group of dogs was used primarily for a study of diuresis by Owen and Ivy,[18] and was subjected to such operative procedures as cannulation of the carotid, trachea and ureters. Nine of the dogs in this group showed an average of one extrasystole every ten minutes over a period of from one to three hours. Records of two to three hours in each of twenty-two dogs (23 per cent) showed only one or two extrasystoles. The remaining dogs (66 per cent) showed no cardiac irregularities other than the normal sinus arrhythmia. In the first group the cardiac irregularities were evident early in the experiment. Thus, in order to eliminate false interpretation of these spontaneously occurring irregularities, all animals used in this study were observed for one-half hour before subjecting them to any procedure for the production of extrasystoles or other cardiac irregularities.

Distention of the Abdominal Cavity.—Since distention of certain of the abdominal viscera leads to stretching of the abdominal wall, it was considered necessary to ascertain if intra-abdominal pressure changes per se would cause cardiac irregularities.

Distention of the entire abdominal cavity was produced in ten lightly barbitalized dogs by the use of an oxygen tank in circuit with a manometer and a small trocar. Intra-abdominal pressure was never allowed to exceed blood pressure more than 5 mm. Distention and deflation in these cases were not productive of cardiac irregularities, although heart rate was increased by distention.

Distention of the Esophagus in Dogs and Rabbits.—Distention of the esophagus was made possible by the insertion and anchoring of a bal-

loon approximately one inch above the hiatus of the diaphragm. In a series of five lightly etherized dogs, distention or sudden collapse of this area even after previous irritation with 5 per cent hydrochloric acid was ineffective in producing cardiac irregularities. On adapting the above procedure to barbitalized rabbits two out of five displayed extrasystoles on either the distention or the deflation. One of these gave an extrasystole on distention when both vagi were severed in the neck and the spinal cord sectioned between the fourth and fifth thoracic vertebrae. Attempts to sever the sympathetic supply to the heart in this animal were unsuccessful.

Sudden Distention of the Stomach.—Distention and sudden collapse of the stomach were obtained by the insertion of a balloon or an open-end cannula, which was tied in place by purse string sutures. In a series of ten barbitalized dogs, distention or sudden collapse after distention

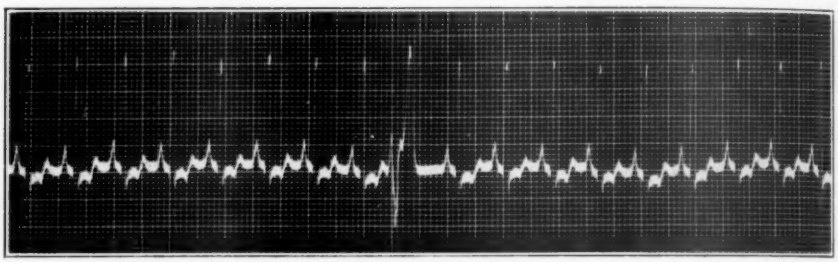

Fig. 1.—This is the electrocardiogram (Lead II) of one of the dogs (Dog M) that showed an extrasystole on belching produced artificially by distending the stomach. Note the extrasystole. The cardiac sphincter must be in tone in order to produce belching, otherwise when the air is injected into the stomach, it passes out of the esophagus.

of the stomach with one or one and one-fifth liters of air caused no cardiac irregularities although the heart rate was either increased or decreased. The response in cardiac rate even varied in the same animal from time to time, the rate generally being increased. In a series of ten lightly etherized dogs results similar to the above were obtained when an open-end cannula was used as an inlet and outlet for air to the stomach. Irritation of the stomach mucosa with 5 per cent hydrochloric acid followed by distention and deflation was not causative of cardiac irregularities in dogs. Adapting the above procedure to barbitalized rabbits, one out of four showed an extrasystole on distention of the stomach.

Belching.—Three out of eleven lightly etherized dogs, in which the stomach was suddenly markedly distended by blowing air into it and in which belching resulted, displayed extrasystoles with each eructation. This was obtained repeatedly in two of the dogs and in one it disappeared after section of the vagi. The vagi were not sectioned in the other two. In the third dog the distention of the stomach with belching caused extrasystoles (Fig. 1) at a frequency of three out of

fifteen trials. In this dog a definite pulsus alternans occurred frequently in periods of three to five minutes during and after distention on a number of trials. Belching could not be obtained unless the cardiac sphincter was in tone because the air passed directly out through the esophagus. When air was blown from the stomach out through the esophagus, extrasystoles did not result. Pilocarpine or epinephrine given to these dogs was without effect.

Because of the results on dogs, a series of twelve medical students who could swallow air and belch at will were studied. Electrocardiograms were made before, during the swallowing of air, and during belching. No cardiac irregularities nor significant changes in rate were observed.

Distention of the Duodenum.—Sudden increase or decrease of intraduodenal pressure in a series of six barbitalized dogs did not cause cardiac irregularities although the heart rate was increased. The rapid injection of 50 c.c. of warm water (39° C.) into the duodenum of ten barbitalized dogs caused no change in the heart rhythm. However, in one of the ten the introduction of 50 c.c. of 0.4 per cent HCl at 39° C. caused a series of extrasystoles. In five lightly etherized dogs after irritation of the duodenum produced by injection of 5 c.c. of 5 per cent HCl, distention failed to cause extrasystoles.

Distention of the Colon.—Marked distention and sudden deflation of the entire colon in six barbitalized dogs caused no cardiac irregularities, although acceleration of the heart rate occurred.

In eight dogs the colon was surgically obstructed, the dogs surviving from one to three weeks. Although the colon became markedly distended and the animals toxic, no cardiac irregularities appeared in the electrocardiograms even as late as one hour preceding death.

Distention and Deflation of the Urinary Bladder.—Sudden distention and deflation of the urinary bladder in five barbitalized dogs did not cause cardiac irregularities. In five dogs under light ether anesthesia the same procedure failed to cause cardiac irregularities even after the irritation of the bladder with 5 per cent HCl.

Distention of the Biliary Passages in Anesthetized Dogs.—Distention of the biliary passages in ten barbitalized and in five lightly etherized dogs failed to produce cardiac arrhythmia. As found by others this procedure simply caused only a decrease or increase in heart rate.

Operative Procedures.—In only one out of eighty-five dogs used in this study did incision of the various viscera cause cardiac arrhythmia. In the one dog an extrasystole resulted on incision of the stomach. The manipulation of the abdominal viscera, such as occurs in abdominal operations, did not cause at any time cardiac irregularities other than a speeding or slowing of the heart rate. The spillage of the contents of the gall bladder, stomach, colon, and urinary bladder into the peritoneal cavity had no immediate notable effect on cardiac rhythm.

Distention of Viscera in the Presence of Spontaneous Extrasystoles.—As was pointed out above, spontaneous extrasystoles occur in 10 per cent of dogs under light ether or barbital anesthesia, when subjected to cannulation of the ureters. Only four dogs out of the eighty-five used in this study showed spontaneous extrasystoles prior to the introduction of procedures which, it was thought, might cause cardiac irregularities. Distention of the various viscera in three dogs did not apparently influence the sequence or frequency of the spontaneously occurring extrasystoles. In one dog, however, distention of the stomach increased the frequency of the extrasystoles sometimes.

ATTEMPTS TO PREDISPOSE OR SENSITIZE THE CARDIAC MECHANISM TO VISCERAL STIMULATION. PART II

It is evident from the preceding results that it is impossible in dogs to induce uniformly, or even frequently, cardiac irregularities other than acceleration or slowing of the heart rate by visceral stimulation. The fact stands, however, that extrasystoles and other irregularities do sometimes result. It is to be noted from the foregoing experiments that chemical irritation of the viscera did not definitely facilitate the elicitation of extrasystoles or other cardiac arrhythmias. It became obvious that if we were to secure cardiac irregularities other than changes in rate more uniformly, it was necessary in some way to sensitize or predispose either the cardiac centers in the central nervous system or the peripheral cardiac mechanism.

Barium Chloride.—Since Pearcy and Howard[16] were able to obtain premature ventricular contractions by visceral stimulation after the administration of cardiotoxic doses of barium chloride, we decided to use this method. They state that when proper care was exercised in giving this agent intravenously, they could obtain cardiac disorders in "practically every animal used" on visceral distention.

We used five barbitalized dogs in which cardiac irregularities failed to appear on gastric distention. When we used the 2 to 8 mg. doses of Pearcy and Howard we failed to obtain premature contractions on distention of the stomach. However, one of the five dogs after receiving 40 mg. showed ectopic beats only on distention of the stomach, which appeared not to be due to the direct effect of the barium. We gave up this procedure because we could not feel absolutely certain that the irregularities one might obtain might not be ascribed to the direct effects of the barium itself on the heart.

Coronary Damage.—It was thought that damage to the left coronary artery might render the heart more susceptible to visceral influences. So, from seven months to one year prior to the visceral stimulation, the heart was aseptically exposed and the ramus descendens of the left coronary was damaged for 2 or 3 cm. along its course by dissecting it free and pinching it with forceps, the dogs being given parathormone

with the hope that an arteriosclerosis might result. (This work was done by Dr. Don C. Sutton who kindly gave me the dogs for my study.) Postmortem studies on the myocardium and the damaged vessels revealed definite pathological changes. Three dogs were available for visceral distention. Distention of the stomach, duodenum, biliary passages, and visceral manipulation failed to elicit cardiac irregularities; however, in one of these dogs distention of both the colon and the urinary bladder caused an extrasystole to occur.

In one of these dogs in which distention of the various abdominal viscera failed to cause an arrhythmia, extrasystoles resulted on dissection of the gastric vagi and on massage of the right stellate ganglion. A "control" series on this procedure was not made.

Experimental Hyperthyroidism.—Since cardiac disturbances are frequently associated with hyperthyroidism, it was decided to feed some dogs thyroid extract for a period prior to the distention of the viscera. Five dogs were fed 5 gm. of thyroid extract daily for a period of one week to ten days. This, of course, caused an increase in respiration and heart rate and a loss of weight and diarrhea. In one of the five dogs distention of the stomach caused extrasystoles, although no irregularities were noted prior to the distention. Distention of the duodenum and urinary bladder did not induce cardiac irregularities in these dogs.

Diphtheritic Myocarditis.—It was reported by Stewart[19] that the injection of diphtheria toxin in appropriate doses would cause a myocarditis in dogs. It was hoped that myocarditis induced by this method would render the heart more susceptible to visceral influences. Five dogs were given 50 to 63 per cent of a minimum lethal dog dose of diphtheria toxin from five days to one week previous to the visceral stimulation. No cardiac irregularities were noted prior to the experiment. Light ether anesthesia was used in some of the dogs and light barbital in the others. In one dog distention and deflation of the stomach caused extrasystoles to appear. In another distention and deflation of the duodenum induced extrasystoles.

Epinephrine, Ephedrine, Pilocarpine and Nicotine.—In a number of dogs in which visceral stimulation failed to excite cardiac irregularities, an attempt was made to predispose the cardiac mechanism by injecting drugs which stimulate sympathetic or parasympathetic nerve endings. These attempts uniformly failed.

Jaundice.—Since biliary tract disease is rather frequently associated with cardiac disturbances[1, 2, 3, 20, 21, 22, 23, 24] and since experimentally only inhibition or acceleration of heart rate usually occurs on distention of the biliary passages of normal anesthetized and unanesthetized dogs (Schrager and Ivy[13] obtained extrasystoles in one of five dogs; Scott and Ivy[12] none in five dogs; and in my work, none in ten dogs), it is possible that biliary tract disease when present for a period of time may in some way predispose the heart to visceral influences. Further,

it is known that jaundice causes a bradycardia in young dogs,[21] and increases vagal tone.[21, 22] Buchbinder[25] observed a transient dislocation of the pacemaker in one dog ten days after the induction of jaundice, and spontaneous arrhythmias in frogs. Hence, it was thought desirable to produce obstructive jaundice in a series of dogs and to ascertain if this condition predisposes to cardiac irregularities on visceral stimulation.

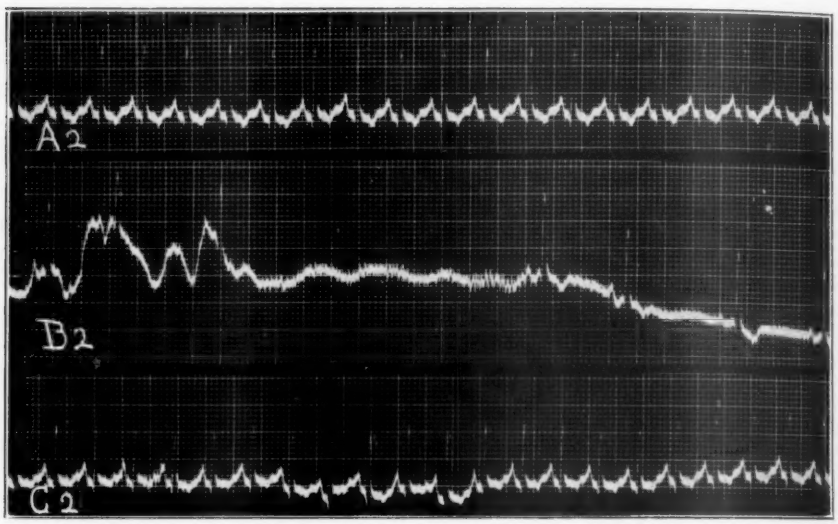

Fig. 2.—These electrocardiograms (Lead II) show a sinoauricular block which occurred (Dog T 11) during the bradycardia associated with vomiting caused by distention of the biliary passages in a dog jaundiced three weeks. A2, one week of jaundice and just preceding distention; B2, bradycardia and S-A block during distention and just after emesis; C2, release of distention.

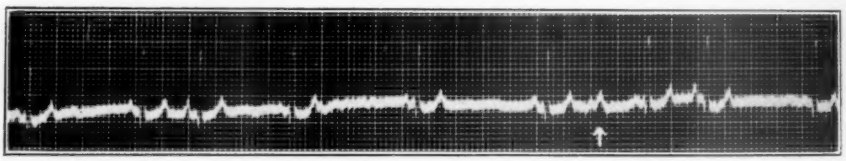

Fig. 3.—This electrocardiogram (Lead II) shows either a bizzare premature QRS complex or an extra-auricular beat, most likely the former, which occurred during a period of slight distention of the biliary passages in a dog (BT10) jaundiced eleven days.

Electrocardiograms were made on a series of five dogs and jaundice produced by aseptic ligation and section of the common bile duct. Electrocardiograms taken at intervals up to two weeks showed in one young dog one week after ligation, a shifting of the pacemaker within the sinus node, which did not exist before operation. Distention of the gall bladder and viscera under light ether anesthesia was performed in four of these dogs with well developed jaundice (one week). A ventricular extrasystole occurred in one on distention of the gall bladder.

In the belief that anesthesia might be a factor, it was decided to repeat these experiments on unanesthetized dogs. So a second series of five dogs with aseptic ligation and division of the common bile duct was prepared. Electrocardiograms (Leads I, II and III) before and after operation showed no cardiac irregularities. The gall bladder was then cannulated aseptically under anesthesia for purposes of distention of the biliary passages. The animals were permitted to recover and electrocardiograms (Lead II) were taken during distention of the biliary passages at various intervals up to three weeks. On distention of the gall bladder all dogs showed changes in cardiac rhythm. Slight distention sufficient to provoke nausea and vomiting always caused a marked

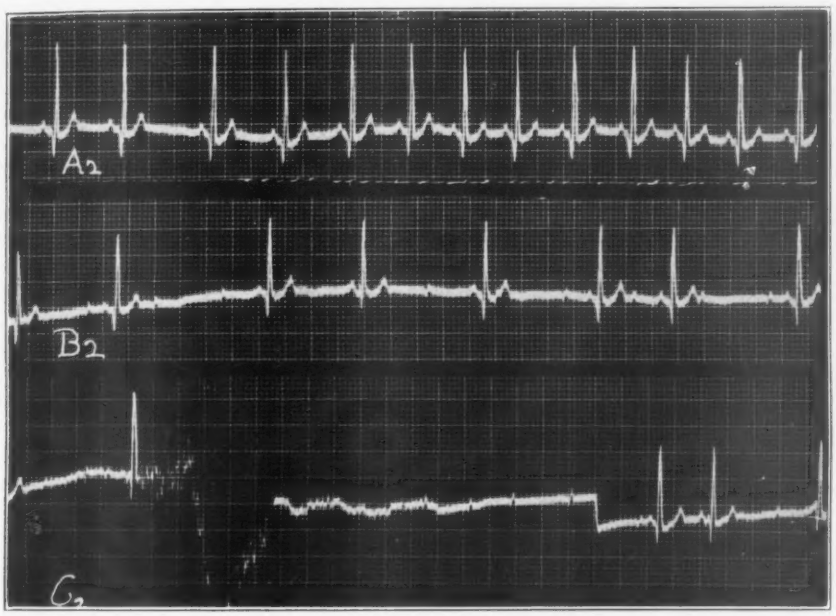

Fig. 4.—These electrocardiograms (Lead II) resulted from a dog (BT12) in which jaundice had been present for three weeks. A2, was taken before distention and is normal; B2, was taken during distention and shows a regularly occurring auricular ectopic beat or A-V block. C2 was taken during gagging produced by distention of the biliary passages and shows an A-V block. Other interpretations have been offered by experienced electrocardiographers.

bradycardia. In one dog a temporary complete sinoauricular block occurred (Fig. 2). In one either a bizzare premature ventricular complex or an ectopic auricular beat (Fig. 3), most likely the former, occurred occasionally during the bradycardia caused by slight distention. In one an ectopic auricular beat occurred during the bradycardia caused by distention and a heart-block (Fig. 4) shortly after retching. Recovery from bradycardia results very soon after release of the pressure and during continued distention the degree of the bradycardia may vary considerably.

SUMMARY AND DISCUSSION

Nine out of ninety-five anesthetized dogs in a group in which the carotid, trachea and ureters had been cannulated showed extrasystoles. Sixty-six per cent of the dogs in this group showed no extrasystoles at any time during the course of the experiment. Since extrasystoles occur "spontaneously" in dogs and in the course of any uniform operative procedure, it is necessary to observe the dog for some time after the necessary operative work has been done before one can determine whether or not a certain procedure will induce extrasystoles. In eighty-five dogs in which the carotid was cannulated and cannulae or balloons were introduced into the various viscera other than the ureters, only four manifested extrasystoles during a half hour observation period following the operative procedures. This does not indicate that the handling of the ureters is prone to lead to extrasystoles, since more visceral manipulation is required to cannulate the ureters than to cannulate or insert a balloon into the duodenum, stomach and gall bladder.

In experiments on eighty-two anesthetized dogs distention and deflation of the hollow organs failed to produce extrasystoles or other cardiac irregularities other than changes in rate. In one dog injection of 50 c.c. of 5 per cent HCl into the duodenum was followed by a series of extrasystoles. In other instances in which an attempt was made to irritate the hollow viscera by the previous injection of acid no cardiac arrhythmias occurred. In one out of eighty-five dogs an extrasystole resulted while holding the stomach with the fingers and incising it with the scissors. Distention of the esophagus produced extrasystoles in two out of five rabbits and of the stomach in one out of four. (The rabbit appears to be more "sensitive" than the dog.) Hence, in the normal unanesthetized dog, cardiac irregularities other than change in rate are very difficult to produce by distention or irritation of the abdominal viscera, but the significant fact is that in a few instances extrasystoles may be produced.

The most interesting observation made in the experiments on this group of animals is that belching caused extrasystoles in three out of eleven animals. Because the esophagus is so closely related to the right auricle it was thought that the extrasystole might be due to mechanical stimulation of the heart by the eructated bolus of air. This was not true in at least one of the dogs, since section of the vagi abolished the phenomenon. Also, in those dogs in which belching could not be produced because of an atonic cardiac sphincter, the rush of air through the esophagus failed to produce extrasystoles, and distention of the lower third of the esophagus was without effect. It appears that the cardiac sphincter must be in tone or the vagus must be hypertonic in order to obtain extrasystoles. However, pilocarpine or epinephrine given to the dogs in these experiments which did not manifest belching failed

to increase the sensitiveness of the mechanism. We believe that belching leads to cardiac irregularities through the same mechanism that is concerned in the production of cardiac irregularities which are associated with retching or vomiting, since belching and retching are closely related phenomena.

It is worthy of note that of the four dogs in which "spontaneous" extrasystoles were present marked distention of the stomach increased the frequency of the extrasystoles in one.

The results of the experiments designed to increase the irritability of the cardiac mechanism to visceral excitation indicate that such is the case. One of these dogs in which previous coronary damage had been produced showed an extrasystole on distention of both the colon and the urinary bladder. Extrasystoles were obtained on visceral excitation in two out of five dogs that had been given a sublethal dose of diphtheria toxin several days previously. Extrasystoles were obtained in one of five dogs previously rendered toxic by the administration of thyroid extract. Of the thirteen dogs used in this group of experiments, extrasystoles occurred in four on visceral excitation only.

The clinical and experimental literature cited above indicates that jaundice, biliary tract disease, or liver injury might lead to a sensitization of the mechanism concerned in the production of cardiac arrhythmias on visceral excitation. In one of ten dogs (one to three weeks), the production of jaundice caused a shifting of the pacemaker within the sinus node. In one of four anesthetized dogs in which jaundice had been present for one week, a ventricular extrasystole resulted on distention of the gall bladder. In five unanesthetized dogs marked and more uniform cardiac arrhythmias resulted on distention of the biliary passages, especially in three of the five. However, the arrhythmias were closely associated with or related in time of occurrence to the production of nausea and vomiting. Although the results indicate that anesthesia depresses and jaundice sensitizes the mechanism concerned in the production of cardiac arrhythmias on distention of the biliary passages, more experiments should be done and an analysis of the relation of nausea (denoted by salivation and smacking of the mouth) and vomiting to cardiac arrhythmias should be made. It was impossible for the author to undertake this phase of the problem, so it was turned over for further study to Dr. Crittenden, whose report will soon follow.

CONCLUSIONS

1. Distention, sudden collapse, or irritation of the hollow abdominal viscera rarely produces cardiac arrhythmias in anesthetized dogs. The fact remains, however, that extrasystoles do occasionally result, a fact which cannot be ascribed to coincidence and which is especially true of eructation of gas from the stomach. In twelve students no cardiac irregu-

larities occurred on belching. Marked distention of the stomach in the presence of preexisting extrasystoles may increase the frequency of their occurrence.

2. The results of experiments designed to increase the irritability of the cardiac mechanism concerned in the production of arrhythmias to visceral excitation indicate that such is the case. This is particularly true of common bile duct obstruction which results in jaundice and liver injury. In three of five jaundiced unanesthetized dogs, distention of the biliary tract caused either an ectopic auricular beat or heart-block, which was generally associated in regard to the time of occurrence with the appearance of retching or vomiting.

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A STUDY OF VISCEROCARDIAC REFLEXES*†

II. The Experimental Production of Cardiac Irregularities in Icteric Dogs With an Analysis of the Rôle Played by Nausea and Vomiting

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THIS study was prompted by the work of Owen,[1] which indicated that marked cardiac arrhythmias may be obtained in icteric dogs following distention of the biliary passages. The occurrence of the cardiac arrhythmias was rather closely related to the appearance of nausea (denoted by salivation and smacking of the mouth) and retching. The experimental and clinical literature has been reviewed by Scott and Ivy[2] and Owen.[1]

In this paper we shall report the results obtained from an electrocardiographic study on unanesthetized dogs and man on the following topics: (1) the effect of apomorphine subcutaneously; (2) the effect of atropine per se intravenously; (3) the antagonistic action of atropine on the action of apomorphine; (4) the effect of jaundice per se; (5) the effect of icterus on the action of apomorphine; (6) the effect of distention of the biliary passage in icteric animals; and (7) the effect of swallowing the stomach tube (ninety-two medical students).

EXPERIMENTAL

In order to determine the effect of vomiting per se on the heart, 0.1 grain of apomorphine was injected subcutaneously. To determine if the effects of apomorphine on the heart were due to vagal action from 0.2 mg. to 1 mg. per kilo body weight of atropine sulphate, dissolved in 0.9 per cent saline solution, was administered intravenously.

Dogs were used for all of the experiments except in those designed to determine the effect of gagging and vomiting caused by the passage of a stomach tube in man. All animals were unanesthetized. The dogs were rendered icteric by aseptically ligating and cutting the common bile duct. The ducts were obstructed ten days prior to the experimental procedure. Ten days were chosen as the best time for the introduction of the various procedures in the icteric dogs, since bile salts are at a maximum concentration in the blood about this time.[5]

Control electrocardiograms were made in all three leads before starting any procedure. All experimental reactions were recorded through Lead II. Care was taken in applying the electrodes to prevent drying

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and to avoid other variations in contact during the course of each experiment. Nausea is clearly indicated in the dog by salivation and smacking of the mouth and swallowing. The dogs were trained to lie quietly and did not move much during vomiting or the other procedures. The electrocardiograms were made under standard and as basal conditions as were possible in this type of work. Of course, the animals were active during retching and vomiting, but nevertheless lay relatively quietly on the table. None of the animals was moribund at the time the experiments were performed.

(1) *The Effect of Apomorphine Subcutaneously.*—Apomorphine was chosen because it causes marked nausea and retching, more marked

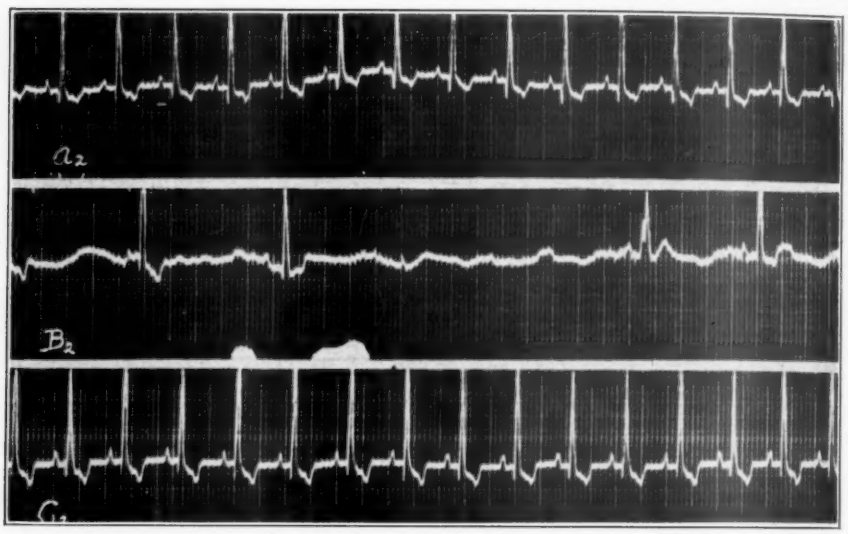

Fig. 1.—Dog No. 11. Normal animal. A_2, control lead two taken before the injection of apomorphine. B_2 is an electrocardiogram taken during retching. It shows a cardiac arrest and a bradycardia. C_2 shows the increase in rate due to nausea.

than that observed on distention of the biliary passages. It was believed that if electrocardiographic abnormalities were associated with nausea and retching, they would certainly occur after the administration of this drug. Thirty normal animals were used in this group. The onset of nausea, after the injection of the apomorphine, usually occurred within one or two minutes. Marked abnormal changes in the electrocardiograms were observed. During nausea an ectopic auricular beat in one animal occurred. Nausea did not occur in two of the animals. In arriving at the following interpretations due consideration was given to artefacts incident to skeletal movements. Certain bizarre changes which occurred when the animal was quiet may have been due to contractions of the stomach incident to vomiting. Such changes were called artifacts.

During retching, fourteen transient heart-blocks (A-V) were observed in eight of the animals; six heart-blocks were observed in one animal;

two in one; and one in six. In seventeen animals of the group, there were thirty cardiac arrests, or complete inhibition of the heart, varying from 1.2 seconds to 2.9 seconds. Nine transient periods of arrests occurred in one animal; five in one; and one each in fourteen. (A cardiac arrest was interpreted as being an inhibition of the heart in which the interval between beats was two or more times as long as the immediately preceding or following beats.) The animal which showed six heart-blocks and nine cardiac arrests also showed "auricular T-waves." A marked bradycardia was noted in one animal, in which the interval between beats was as long as 1.6 seconds to 2.1 seconds. An ectopic P-wave occurred once. In one animal, retching did not occur.

During vomiting, ectopic ventricular beats occurred in one animal and a pulsus bigeminus with ectopic ventricular beats in another.

Rate: Changes occurred in the P- and T-waves and in the QRS complex in a number of the animals, but nothing of a characteristic nature was noted. Nausea caused an average increase in the heart rate of 98 beats per minute (+6 to +186). Retching caused an average decrease of 126 (0 to −232). Immediately following vomiting the rate returned to the "nausea" rate. The rate changes were determined by comparison with the immediately preceding rate.

Summary.—These results show that rather marked electrocardiographic changes are associated with nausea, retching and vomiting. The changes are most marked during retching.

(2) *The Effect of Atropine per se Intravenously.*—Fourteen animals were used in this group. They received atropine sulphate intravenously. Two of them received 1 mg. per kg., the others from 0.2 mg. to 0.33 mg. per kg. The former dosage caused an increase in rate of 204 per minute. The other dosages caused an increase of from 36 to 174 with an average of 96 beats per minute. No marked changes in the electrocardiograms were noted following the atropine.

Changes in the P-wave: Seven animals did not show any change in the form of the wave. The remainder showed briefly the following changes: a maximum increase in the voltage of 1 mm. or a decrease in the voltage of 1 mm.; the wave became negative or was occasionally absent or diphasic; or the P- and T-waves fused.

Changes in the QRS complex: Five animals did not show any change in the form of the complex. The changes noted in the other animals were briefly as follows: an increase in R voltage of 6 mm. in two; a decrease of from 2 mm. to 6 mm. in four; a decrease in Q voltage in one; an increase in Q voltage in one; and the notching of R in one.

Changes in the T-wave: Six animals did not show any change in the T-wave. The following changes were noted in the other animals: the voltage increased 3 mm. in one; it became negative in two; occasionally negative in two; diphasic in one; occasionally diphasic in one; the wave disappeared in one; became occasionally absent in two; and absent in one.

(3) *The Antagonistic Action of Atropine on the Action of Apomorphine.*—Eleven of the animals in the above group were given apomorphine within two to five minutes after the injection of the atropine. The appearance of nausea was greatly delayed and often did not occur for from ten to fifteen minutes after injection. The phenomena of marked cardiac inhibition and heart-block did not occur in these animals. No nausea occurred in six animals; no retching in one; and no vomiting in one. A few changes in the P- and T-waves and in the QRS complex were noted, but they were not characteristic.

Rate: During nausea the heart rate showed an average increase of 53 beats per minute (+24 to +90); during retching it was decreased only 10 (−29 to + 22); and during vomiting it increased 21 (−18 to +102).

Summary: These results clearly indicate that the pathway concerned in causing the electrocardiographic changes in the heart which are associated with nausea, retching and vomiting produced by apomorphine

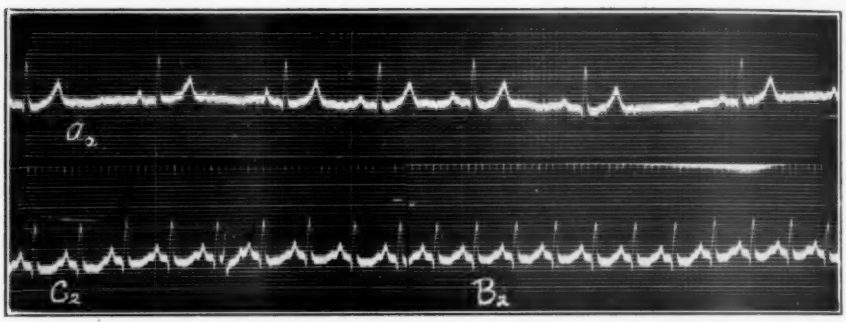

Fig. 2.—Dog No. 10. Normal animal. Lead II. A_2 is the control electrocardiogram taken before the injection of 1 mg. per kg. of atropine sulphate. B_2 shows the effect of the atropine. C_2 was taken during nausea after atropine and apomorphine. An adventitious wave is seen which was interpreted as an artefact.

is via the vagus nerves. The tachycardia of nausea must be due to both increased activity of the sympathetic or accelerator mechanism and a decrease in vagal inhibitory tone, since apomorphine alone caused an average increase in heart rate of 98 beats per minute and after atropine an average increase of 53 beats.

(4) *The Effect of Icterus per se.*—Sixteen animals were used in this group. Control electrocardiograms were made before ligation and section of the common bile duct, and again ten days later before cannulation of the gall bladder for the purpose of distending the biliary passages. The degree of icterus in these animals varied as determined by the inspection of the sclera and subcutaneous tissues at the time of operation. All, however, were definitely icteric. According to these observations, two animals were slightly icteric; two were slightly to moderately icteric; seven were moderately icteric and five were markedly icteric.

Abnormal beats, which could be ascribed only to icterus, appeared in three animals. Ectopic ventricular beats were found in two; extra-

auricular in one. Some of the abnormal beats which were present before icterus, disappeared with icterus. These were the disappearance of "spontaneous" heart-block, or a rhythmically occurring auricular ectopic beat in two, and an extrasystole in one.

Rate: There was no change in rate in one. The rate was increased from 12 to 84 beats per minute in eleven and decreased from −6 to −72 in four. The rates were determined from the electrocardiograms only after a period of quiescence on the table.

Changes in the P-wave: No change occurred in Lead I in eight of the group. This wave became absent in four and negative in one.

No change occurred in Lead II in twelve animals. The wave became absent in one, negative in one, notched in one; a decrease in voltage was noted in three; and an increase in voltage up to 4 mm. was noted in one.

No change in the wave occurred in Lead III in ten animals. The wave became absent in one, negative in one, diphasic in one, and positive in one. The P-wave did not disappear from all three leads in the same dog.

Changes in the QRS complex: No change in Lead I was observed in four animals. Other changes were: a decrease in R voltage of 8 mm. in four, an increase up to 9 mm. in seven, and an increase in Q voltage in three.

No change in the form of the complex occurred in Lead II in two animals. Other changes noted were: an increase in R voltage up to 10 mm. in three; a decrease up to 11 mm. in one; an increase in Q voltage in three; a decrease in one; and the slurring of R in one.

No change was observed in the form of the complex in Lead III in four animals. Other changes noted were: the R became slurred in one, and notched in one; there was an increase in R voltage up to 13 mm. in four and a decrease up to 7 mm. in eight; and an increase in Q voltage in three.

Changes in the T-wave: No change in the form of the T-wave was observed in Lead I in five animals. The wave became absent in three, negative in one, and positive in one.

No change in the form of the wave was observed in Lead II in four of the animals. Other changes noted were: the wave became absent in two; positive in three; negative in four; diphasic in two; notching disappeared in one; there was an increase in voltage in one and a decrease in voltage in one.

No change in the form of the wave was observed in Lead III in four animals. The wave became absent in two, positive in two, negative in five, diphasic in two; and notching disappeared in one.

Summary: Icterus caused electrocardiographic irregularities to appear in three of the sixteen animals and to disappear in three. Various changes also occurred in the different waves in the three leads. The changes were so variable that we hesitate to interpret them.

(5) *The Effect of Icterus on the Action of Apomorphine.*—We desired

to ascertain whether icterus made dogs more sensitive to apomorphine in regard to the electrocardiographic irregularities associated with nausea and vomiting. Fourteen animals were used in this group. All of them were given apomorphine before obstruction of the common bile duct as a control. Eleven received apomorphine after production of icterus but before cannulation of the gall bladder and the others after either the first or second distention of the biliary system. The degree of icterus in these animals was determined as was noted above. Two animals were slightly icteric; two slightly to moderately icteric; four moderately icteric and six markedly icteric.

Nausea was not observed in four of these animals after apomorphine, and no abnormal beats were observed in the others during nausea. The

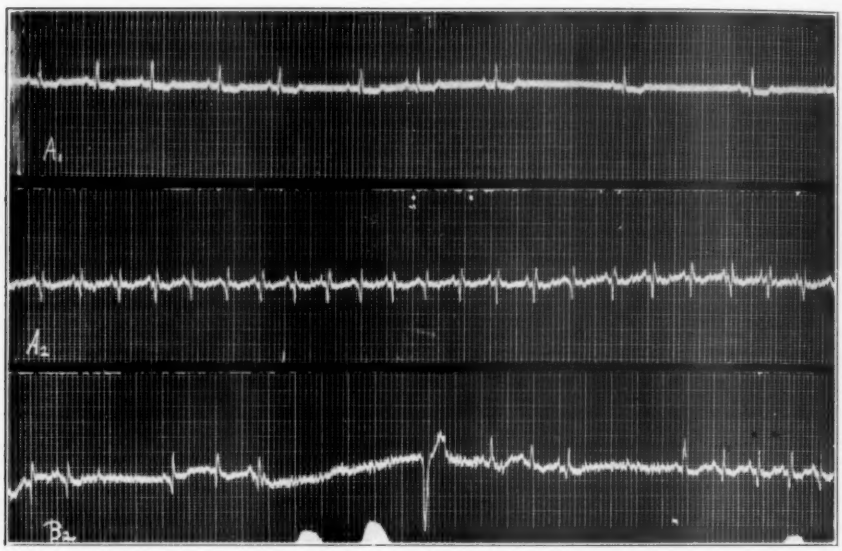

Fig. 3.—Dog No. 29. Moderately icteric. Lead II. A_1 is the control electrocardiogram taken before cannulation of the common bile duct. There is a sinus arrhythmia. A_2 is the control electrocardiogram taken ten days after ligation of the bile duct. It shows an increase in rate and possibly somatic tremors, although the dog was not visibly trembling. B_2 shows the effect of retching, following apomorphine in the icteric animal. It shows a return of the arrhythmia and an ectopic ventricular beat.

explanation of the absence of nausea in the four animals is not clear, especially since the onset of retching was not delayed. It is possible that icterus may depress the nausea mechanism in certain individual animals, since some animals appear to be depressed.

During retching five animals showed eight transient periods of A-V heart-block as compared to three periods of heart-block in three animals before they were icteric. There were fourteen cardiac arrests in ten animals as compared to eight arrests in seven animals before the production of icterus. Four of the five animals had not shown heart-blocks previously, and five of the ten had not shown cardiac arrests before icterus. One animal showed a high grade block with "auricular T-waves,"

and another animal manifested interpolated beats. In another animal there were ectopic ventricular beats in which the R-wave was absent, the S voltage was 22 mm. and the following T voltage 8 mm. (Fig. 3).

During vomiting one animal showed interpolated beats and two a marked bradycardia after vomiting instead of the previously existing tachycardia of nausea.

Rate: Nausea caused an average increase in the rate of 72 beats per minute (+25 to +126). Retching caused an average decrease of 102 (−46 to −140); and vomiting an average increase of 115 beats per minute (+59 to +153). These changes were in general less than those observed in nonicteric animals. Changes in the form of the various waves occurred in a number of animals, but nothing of a characteristic nature was observed.

Summary: The changes noted in this group of animals did not parallel the degree of icterus of the sclera and subcutaneous tissue. However,

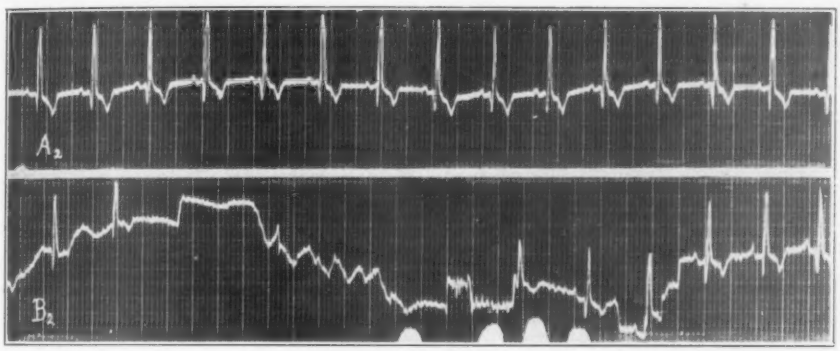

Fig. 4.—Dog No. 14. Markedly icteric. Lead II. A_2 is the control electrocardiogram taken before the distention of the biliary system. The inverted T-wave is normal for this dog. B_2 shows a cardiac arrest (3.36 seconds) due to severe pain (no retching was observed) caused by distention of the biliary system.

the changes indicate that icterus does "sensitize" the heart to the electrocardiographic abnormalities associated with retching. This statement is based primarily on the comparison of the marked abnormal cardiac changes noted above.

(6) *The Effect of Distention of the Biliary Passage in Icteric Animals.*—A control series on the effect of distention of the biliary passages in nonicteric dogs was not studied by us since in this laboratory a series of twenty dogs has been studied electrocardiographically. Extrasystoles occurred in only one of this group, only a tachycardia or a bradycardia being otherwise observed.

Fifteen animals were used in this group. They were rendered icteric by ligating and sectioning the common bile duct. The biliary system was distended ten days later by injecting from 40 to 100 c.c. of warm water through a syringe into the cannulated gall bladder. Because icterus increased the friability of the biliary system, satisfactory results

on distention, i. e., without leakage around the cannula, were obtained in only six animals. Three of these were moderately icteric, and three markedly icteric. In three of the animals the biliary system was distended a second time, on the day following the first distention. The cannula began to leak at this time. Hence the results in this group refer to nine distentions in six animals. This adds six animals to the series of Owen.[1] No nausea occurred in two distentions, no rechting in six, no vomiting in three, and no apparent pain in three.

A cardiac arrest occurred in one animal after vomiting, and in another during pain (Fig. 4). Ectopic ventricular beats were noted in three animals during pain and in another during nausea. An extrasystole occurred in one animal during nausea and in another during pain. In one of the markedly icteric animals, the heart stopped for 2.16 seconds during marked pain. Late during the period of continued distention, after the pain, nausea, retching and vomiting responses were no longer acutely manifest, cardiac irregularities were rare. The various waves were studied carefully, but nothing of a characteristic nature was noted.

Rate: Mild distention either increased or decreased the rate; the average decrease was 30 beats per minute and the increase 27. The effect of nausea on the rate also was variable. Retching decreased the rate from 15 to 36 beats per minute. During and just after the act of vomiting, the rate was either decreased or increased. Pain was associated with a decrease or increase in rate (−36 to +42). Following distention the rate varied. It usually returned to normal within about five minutes.

Summary: Changes in this group more closely parallel the degree of icterus than did those noted above in the icteric animals receiving apomorphine, probably because distention of the biliary passages is a submaximal stimulus. Owen[1] studied the electrocardiographic changes on distention of the biliary system in icteric animals, and observed the same marked changes which we observed in this group of animals. He thought that the presence of preexisting icterus in dogs sensitizes the mechanism concerned in the elicitation of cardiac irregularities. Our results, we feel, add further evidence that icterus may sensitize the cardiac vagal mechanism. Since the cardiac irregularities were associated primarily with pain, vomiting or retching, and were not observed during continued distention when there were no objective manifestations of acute pain and retching, and since atropine abolishes most of the irregularities, these irregularities must be due to a motor discharge sent out over the vagi as the consequence of acute pain sensations and particularly of the sensory impulses which provoke retching.

(7) *The Effect of Nausea and Retching Produced by Swallowing the Stomach Tube in Man.*—Of the ninety-two students who swallowed the stomach tube in these experiments, eleven did so with no difficulty (no gagging), fifty-nine with difficulty (gagging), and twenty-two with marked difficulty (gagging and vomiting). In these students the con-

trol electrocardiograms showed ventricular extrasystoles in two, and ectopic ventricular beats in another.

During the passage of the stomach tube, A-V blocks occurred in three.

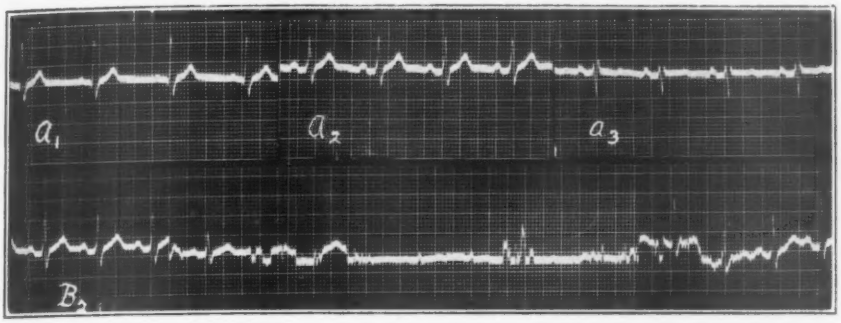

Fig. 5.—Student B. A_1 and A_2 and A_3 are the control electrocardiograms in all three leads taken before swallowing the stomach tube. B_2 shows a prolonged ventricular standstill, and a possible A-V block, which occurred during gagging while swallowing the tube. The student felt faint and dizzy.

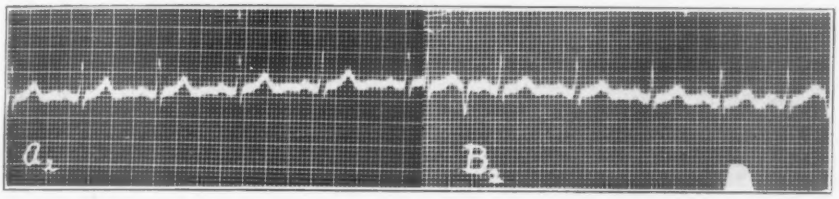

Fig. 6.—Student S. Lead II. A_2 is the control electrocardiogram. B_2 was taken while the student was swallowing the stomach tube and shows ectopic beats which occurred during gagging and just after the T-wave each time.

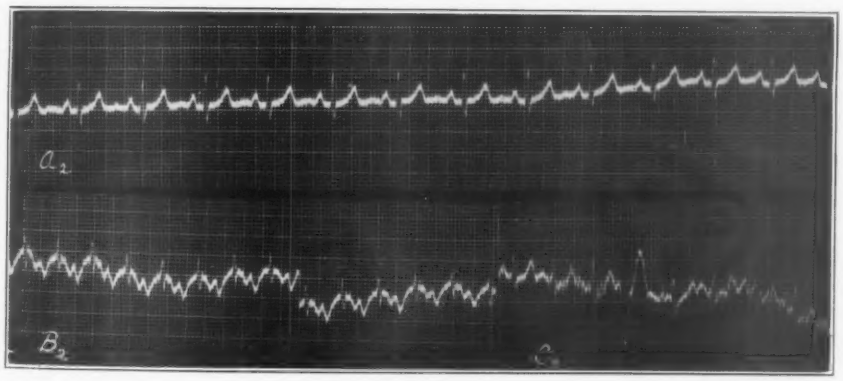

Fig. 7.—Student K. A_2 is the control electrocardiogram. B_2 was taken while the student was swallowing the stomach tube and shows primarily an increase in rate, which occurred early soon after the tube was started. (The film was inverted by the photographer.) C_2 shows a ventricular extrasystole which occurred during gagging.

In one of the students the ventricular arrest was so prolonged that six seconds elapsed between normal ventricular beats. Ventricular extrasystoles were noted in one and an extrasystole of auricular origin in two. Ectopic ventricular beats were noted in five.

The various waves were studied carefully but nothing of a characteristic nature was detected.

Rate: No change in rate was observed in one student who had no difficulty in swallowing the tube. The rate was increased 28 (average) beats per minute (+6 to +72) with no gagging, increased 41 (−6 to +79) with gagging, and 45 (+16 to +78) with vomiting. It is interesting that only one student manifested inhibition during gagging, which stands in marked contrast to the dogs.

DISCUSSION

The results, following the injection of apomorphine in normal animals, show that nausea, retching and vomiting (especially retching) cause marked cardiac irregularities. Not only do changes in rate occur, but also changes in the form of the various waves, heart-block, and arrest result.

Since it is known that stimulation of the peripheral end of the vagus not only affects the rate of the heart, but also impairs conductivity and may produce A-V blocks, it was reasonable to assume that the changes incident to nausea and vomiting might be abolished by atropine. This proved to be true. These changes indicate that when the vomiting center, or nausea mechanism, is strongly excited, along with the motor discharge that passes out to the stomach from the vagus center, a discharge arises from the cardio-inhibitory center which passes to the heart via the vagi and markedly modifies cardiac activity. A maximum excitation of the vomiting center must be present before the cardio-inhibitory center is sufficiently affected to produce heart-block, since the nausea and vomiting induced in nonicteric dogs by distention of the biliary passages does not cause marked changes. Apomorphine in the doses used certainly produces maximum excitation of the center.

Since bile salts increase the tone of the vagus, it was thought that icterus would increase the cardiac irregularities after apomorphine and after distention of the biliary passages. Our results indicate that this is the case.

Icterus per se gave variable results. We had expected more irregularities due to icterus without the introduction of an additional factor. It was noted that cardiac ectopic beats occurred after icterus, but in some of the animals such beats disappeared after the animals were icteric. The accentuation of the sinus arrhythmia as reported by Buchbinder[4] and anticipated by us was not observed. The rate changes were not consistent, as was found by Buchbinder,[4] but the tendency was toward an increase in the majority of animals. Although we were not certain of the ages of the animals, the four in which the rate was decreased were relatively young dogs. The depth of the icteric coloration of the sclera did not parallel the extent of the cardiac irregularities.

The results, in the icteric animals receiving apomorphine, showed more

cardiac irregularities than were noted before the animals became icteric. If icterus sensitizes the vagal mechanism as we believe, then our results are in accordance with such a hypothesis. Although the irregularities did not parallel the degree of icterus, it must be kept in mind that apomorphine is a maximal stimulus in producing nausea, retching and vomiting. With a submaximal stimulus, as we shall see below, the results do parallel the degree of icterus.

The distention of the biliary system caused nausea, retching, vomiting and pain. These symptoms were associated with cardiac irregularities which closely paralleled the degree of icterus as was expected. Schrager and Ivy,[3] Scott and Ivy,[2] and Owen[1] in the distention of the biliary system of twenty unanesthetized and nonicteric animals observed cardiac ectopic beats in only one animal which may have had a "sensitive" heart to begin with. Our results when compared with theirs support the hypothesis that icterus sensitizes the cardiac vagal mechanism. Owen, however, in the distention of a group of anesthetized icteric animals failed to obtain cardiac irregularities which he and we observed in unanesthetized dogs. This difference is obviously due to the fact that anesthesia depresses the vomiting reflex.

The results on the students are especially interesting when compared to the results obtained in the first group of animals receiving apomorphine. It was noted that the rate changes in the dogs were much more marked than those in the students. Only one student showed a decrease in rate and this was very slight, while in the dogs nausea and vomiting were accompanied by a tachycardia and retching by a bradycardia. Two factors may play a rôle in these differences. The stimulus used for the dogs was maximal (apomorphine) while that for the students was submaximal. Also the origin of the reflex in the dogs (distention of bile passage) was abdominal while in the students it was pharyngeal. The origin of the reflexes may play a rôle even though the end-result, nausea and vomiting, are the same. However, the results on the students are more analogous to the results obtained in nonicteric dogs on distention of the biliary passages.

The abnormal beats observed in the students indicate that "sensitive" hearts may react to swallowing the stomach tube. It would seem that if the retching were marked, in some instances it might be serious. For instance, the student in whom there was a prolonged ventricular standstill, reported that he felt very ill and dizzy while swallowing the tube. It seems possible that such an arrest may be sufficiently prolonged in certain cases to prove fatal. Recently there have been reported to us two cases of sudden death on passage of a stomach tube. One was a postoperative case of carcinoma of the stomach, which was to be treated by lavage. The passage of the stomach tube resulted in sudden unexplained death. The other case had carcinoma of the cardia with an angina pectoris. In this patient an attempt was made to secure gastric contents

for a gastric analysis. During passage of the stomach tube, the patient stated that he felt very ill, and as the tube was being withdrawn, he died.

SUMMARY

The results of this study seem to indicate clearly that nausea, retching and vomiting (induced by the subcutaneous injection of apomorphine) may cause in normal unanesthetized dogs cardiac irregularities, such as heart-blocks, cardiac arrests, ventricular and auricular ectopic beats. These are most likely to occur during retching. There were also changes in rate, nausea causing usually a tachycardia and retching a bradycardia.

The intravenous injection of atropine almost completely inhibited the cardiac irregularities associated with nausea, retching and vomiting following the injection of apomorphine. The results indicate that during marked excitation of the vomiting center the cardio-inhibitory mechanism is affected, the degree to which it is affected depending upon its sensitivity.

Icterus per se caused both the appearance and the disappearance of electrocardiographic abnormalities in a few instances. The changes in rate were variable, but the tendency was towards an increase. Slowing of the heart rate, however, may occur. Preexisting icterus increased the occurrence of the cardiac irregularities which are associated with the elicitation of nausea, retching, vomiting and pain by distention of the biliary passages. The irregularities following the injections of apomorphine could not be said to parallel closely the degree of icterus; but the changes due to distention of the biliary system did parallel the degree of icterus. This may have been due to the probable fact that apomorphine is a stronger stimulus. The results of the experiments on the icteric animals, we believe, indicate that icterus sensitizes the cardiovagal mechanism.

Electrocardiographic abnormalities, such as extrasystoles, arrests, ectopic, ventricular, A-V blocks, etc., occurred in 10 per cent of the students while nauseated or retching during the swallowing of a stomach tube. No change in the rate was observed in one student. In the others there was an increase in rate which was dependent upon the ease with which the tube was swallowed. It is interesting to note that a bradycardia did not occur, whereas in dogs during retching bradycardia occurred very uniformly.

In all experimental procedures, changes in the P-wave, the QRS complex and the T-wave occurred, none of the changes being characteristic.

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THE SIGNIFICANCE OF LARGE Q IN LEAD III OF THE ELECTROCARDIOGRAM DURING PREGNANCY

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Pardee[1] has called attention to the occurrence of a large Q-wave in Lead III of the electrocardiogram. Briefly he defined it as a Q-wave in Lead III 25 per cent or more of the largest excursion of the QRS in any lead. He found this condition present in 7 per cent, or fourteen of 200 cases of heart disease of various sorts. Eight of his fourteen examples of deep Q_3 occurred in thirty patients who had the anginal syndrome. The remaining six records showing deep Q_3 were distributed among 170 patients suffering with heart disease other than angina. In a series of 277 records from normal hearts which he also reported only two showed the condition. Pardee also observed that a large Q_3 could occur during pregnancy and disappear after delivery and that it was profoundly affected by respiration. Nevertheless, he concluded that a deep Q_3 represents an impairment of the left ventricle, in most instances due to coronary narrowing. Willius[2] concurred in these views. He found 300 records which showed deep Q_3. Of these 300 records, 89.3 per cent "were obtained in examination of patients who had one of the following conditions: hypertensive heart disease, the anginal syndrome, hypertensive heart disease accompanied by the anginal syndrome, or arteriosclerotic heart disease not accompanied by the anginal syndrome or hypertension." There were only three cases, or 1 per cent, in which the patients had normal hearts. In a group of 977 normal patients, only two cases, or 0.2 per cent, showed large Q_3. Therefore, Willius believes deep Q_3 to be an additional diagnostic sign of heart disease. Fenichel and Kugell[3] made observations which corroborated this work. They also correlated the electrocardiographic and post-mortem findings in thirty-five cases. Twenty-seven cases showed at post-mortem examination myocardial fibrosis or infarction; seventeen of these twenty-seven had shown large Q_3 in electrocardiograms, only ten did not show large Q_3. In the remaining eight cases electrocardiograms had shown no large Q_3 waves, and there was no evidence of myocardial damage at post-mortem.

While studying axis deviation of the electrocardiogram during the

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course of pregnancy, we selected those records which showed a large Q_3 strictly according to the criteria of Pardee.[1] The criteria are: (a) that Q_3 should be 25 per cent or more of the greatest deflection from the base line of the QRS complex in any lead; (b) that no records should have R_3 greater than R_2, none should show right axis deviation; (c) that an R_3 must be present; (d) that S_3 must be absent; (e) that no "vibratory" or irregular QRS complexes of the "M" or "W" types in Lead III should be present. We have separated those records which show a deep Q_3 wave only transiently, appearing and disappearing apparently with phases of respiration. A deep Q_3 selected according to these criteria was continuously present in the records from 17 of 342 cases. It occurred transiently in the records of 9 additional cases. Counting only the 17 in which the sign was continuously present, the incidence of deep Q_3 in our series is slightly less than 5 per cent as compared with 7 per cent in Pardee's 200 cardiac patients[1] and 0.42 per cent of approximately 70,000 records searched by Willius.[2]

Our series is made up of electrocardiograms taken from pregnant women referred privately or to the cardiac clinic of the Boston Lying-in Hospital for estimation of their cardiovascular status. The diagnoses in the 342 patients whose electrocardiograms were studied were as follows: rheumatic heart disease was diagnosed sixty-six times, congenital heart disease five times. There were two patients with hypertension and one with active rheumatic infection and one with questionably active rheumatic infection. In twenty-three cases there were extremely loud systolic murmurs, loudest at the base especially in the pulmonic area, which seemed too intense to be functional and yet on careful consideration could not definitely be diagnosed as either congenital or acquired heart disease. We suspect that these murmurs are associated with the changing position of the heart during pregnancy. The remaining 244 cases showed no cardiac pathology. To be sure, all of these 244 patients were referred to the heart clinic of the hospital for an opinion because they had signs or symptoms which suggested the possibility of heart disease to the house officers in the routine admission physical examination. The signs and symptoms which attracted their attention were systolic murmurs, moderate or faint at the base, and best heard in the pulmonic area; reduplicated first or second sounds; simple sinus tachycardia; or extrasystoles. A few had a story of mild palpitation which may have been paroxysmal tachycardia. Complaints of vague palpitation, breathlessness, night starts and a sense of weakness also served to send some of the patients in this group to the heart clinic. In none of these 244 patients was organic heart disease found. The signs and symptoms merely arrested the attention of the routine examiner who referred the patient for special examination. The group cannot, in any way, be considered a group of patients with abnormal hearts. They were examined carefully to determine whether they had heart disease and were

found to have none. They are, therefore, more clearly a normal group so far as their hearts are concerned than would be any unselected group of pregnant women.

In Table I are tabulated the 17 cases, the records from which showed deep Q_3 continuously present. Among these, there was one patient with definite rheumatic mitral stenosis, one with questionable rheumatic mitral regurgitation, and one with active rheumatic infection, that is, two or at the most three cases of organic disease in the 17 showing a deep Q_3-wave in all complexes of Lead III. One patient died of eclampsia post partum, but there was no evidence of eclampsia when the electrocardiogram was taken. In the remaining 13 patients there was no organic cardiac pathology. There was no evidence of the anginal syndrome in any patient in this series.

Should a deep Q_3 be related to organic change in this series, we would expect to find evidence of such change present in a greater number of those patients whose electrocardiograms exhibited the deep Q-wave in all complexes of Lead III. Only 17.6 per cent of the seventeen patients continuously showing deep Q_3 had organic heart disease, while in the series as a whole 21.6 per cent were diagnosed as having definite organic cardiac change. To present the results even more clearly:

Among 98 patients with organic or doubtful heart disease deep Q_3 was found 3 times (3 per cent).

Among 244 patients with no heart disease deep Q_3 was found 14 times (5.7 per cent).

All but six of the seventeen electrocardiograms which continuously showed deep Q_3 were taken in the sixth month of pregnancy or later. Like Pardee[1] we found that R_1 was greater than R_2 in the majority of the cases showing deep Q_3. In one of them R_1 equaled R_2, the Q- and R-waves in Lead III nearly balancing each other. The presence or absence of the various waves and the positive or negative quality are indicated in Table I. The finding of greatest significance is that T_3 is inverted in sixteen cases and is flat in the remaining one. Of almost equal importance and of similar significance, as will be discussed below, is the fact that in twelve of the seventeen cases P_3 is variable, that is, positive, negative or iso-electric. The P-wave is flat in one and upright in only four. The actual axis deviation according to the criteria which we use (White[4]) was normal except for one instance of left axis deviation.

In Table I are also tabulated the nine cases showing marked variation of Q_3, presumably respiratory. At its least value Q_3 is less than 25 per cent of the greatest QRS in any lead of the same electrocardiogram, or absent entirely, while at its greatest it is at least 25 per cent of the maximum QRS in any lead of the same electrocardiogram. These nine cases are not grouped with the seventeen just discussed because the deep Q_3 was not continuously present. They show that deep Q_3 in some cases is in-

TABLE I* (See footnotes on opposite page)

SERIES	DIAGNOSIS	MO. OF PREGNANCY	LEAD I					LEAD II					LEAD III					$R_1=R_2$	$R_1>R_2$	$R_2>R_1$ OR R_3	AXIS DEVIATION	OUTCOME	
			P	Q	R	S	T	P	Q	R	S	T	P	Q	R	S	T					MOTHER	BABY
1	No Ht. Dis.	6	+		+	+	+	+		+	+	+	θ	+	+		−		+		Normal	Good	Good
2	No Ht. Dis.	8	+		+	+	+	+		+	+	+	+	+	+		−	+			Normal	Good	Good
3	No Ht. Dis.	5	+		+	+	+	+		+	+	+	θ	+	+		−		+		Normal	Good	Good
4	Rheum. Ht. Dis. M.S.	7	+	+	+		+	+	+	+		+	θ	+	+					+	Normal	Good	Good
5	No Ht. Dis.	6	+		+	+	+	+		+	+	+	θ	+	+		−		+		Normal	Good	Good
6	?Rheum. Ht. Dis. M.R.	5	+		+	+	+	+	+	+		+	+	+	+		−			+	Normal	Good	Good
7	No Ht. Dis.	3	+		+	+	+	+	+	+	+	+	+	+	+		−			+	Normal	Good	Good
8	No Ht. Dis.	6	+		+	+	+	+		+		+	θ	+	+		−		+		Normal	Good	Good
9	No Ht. Dis.	7	+		+	+	+	+	+	+		+	+	+	+		−			+	Normal	Unknown	Unknown
10	No Ht. Dis.	7	+		+	+	+	+		+	+	+		+	+		−			+	Normal	Good	Good
11	Irrit. Ht.	8	+		+	+	+	+		+	+	+	θ	+	+		−		+		Normal	Good	Good
12	No Ht. Dis.	5	+		+	+	+	+		+	+	+	θ	+	+		−		+		Left	Good	Good
13	S.A. Tachycardia	8	+		+	+	+	+	+	+	+	+	θ	+	+		−			+	Normal	Good	Good
14	Effort syndrome	7	+		+	+	+	+		+		+	θ	+	+		−		+		Normal	Living and well	Premature baby died
15	No Ht. Dis.	4	+		+	+	+	+		+	+	+	θ	+	+		−		+		Normal	Good	Good
16	Parox. Tachycardia	6	+		+	+	+	+		+	+	+	θ	+	+		−		+		Normal	Good	Good
17	Rheum. fever	4	+		+	+	+	+		+		+	θ	+	+		−		+		Normal	Died Postpartum Eclampsia	Died
	Records Showing Respiratory Variations																						
1	No Ht. Dis.	6	+		+	+	+	+		+	+	+	θ	θ	+		−	+			Normal	Good	Good
2	No Ht. Dis.	8	+	+	+	+	+	+	+	+	+	+	θ	θ	+		−			+	Normal to left	Good	Died
3	No Ht. Dis.	7	+		+	+	+	+		+	+	+	θ	+	+				+		Normal to left	Good	Good
4	Rheum. Ht. Dis. M.S.	8	+		+	+	+	+	+	+	+	+	+	+	+			+			Normal	Good	Good
5	No Ht. Dis.	5	+	θ	+	θ	+	+	+	+		+	+	+	+		−		+		Normal	Good	Stillborn
6	No Ht. Dis.	7	+		+	+	+	+		+	+	+	θ	+	+		−		+		Normal	Good	Good
7	No Ht. Dis.	8	+		+	θ	+	+		+		±	θ	+	+		−			+	Normal	Good	Good
8	No Ht. Dis.	4	+		+	+	+	+		+		+	−	+	+		−		+		Left (Inv. L III)	Good	Good
9	No Ht. Dis.	8	+	+	+	+	+	+	+	+		+	o	o	+		−			+	Normal	Good	Good

constant and freely variable. We wish to call attention particularly to the following findings: in seven of these nine cases T_3 is inverted and in the other two is flat. P_3 is inverted in one case, varies from inverted to slightly positive in six and is upright in two. The axis is normal in six, shows left deviation in one, and varies from normal to left in two. In all except two the electrocardiograms were taken in the sixth month or later.

DISCUSSION

In our opinion, these findings in pregnant women indicate that a large Q_3 may result from a change in position of the heart. This may arise from a more transverse position of the heart or from rotation of the heart on its own long axis or a combination of these two. Several contributions to the literature concerning the influence on the electrocardiogram of the position of the heart in space are of interest in this connection. Cohn[5] by rotating the leads of the electrocardiogram taken directly from the chest in a clockwise manner 80 and 120 degrees produced curves showing typical large Q_3-waves. He points out that these electrocardiograms are essentially those of left axis deviation as would be expected from the angle of the heart in respect to the rotation of the Einthoven triangle. It is important, however, that these artificial curves differ from true left axis deviation in one respect, the P_3- and T_3-waves are inverted, i. e., are in the same direction as the QRS complex in Lead III. This corresponds to the result of Bland and White's study[6] of complete inversion of Lead III due to transverse position of the heart. Findings of similar significance in regard to the inverted T-wave in Lead III associated with left axis deviation comes from studies on the electrocardiogram in obesity.[7, 8] This evidence from the literature points to the possibility that inverted T_3 and P_3 are characteristic of transverse position of the heart. In our experience inverted T_3 and low, iso-electric, inverted or variable P_3 are commonly associated with the presence of large Q_3 (see Table I).

Our findings in pregnant women, both with and without heart disease, in whom we relate the occurrence of deep Q_3 to the transverse position of the heart, suggest that in nonpregnant patients a deep Q_3 may be associated with a particular body type, characterized by a relatively short, thick trunk and high diaphragm (a type traditionally subject to degenerative vascular disease), rather than with organic change in the heart muscle itself. Certainly a sign which can so readily be produced by change in position of the heart would seem to be unreliable as an aid in the diagnosis of organic disease of the myocardium.

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*This table gives the details of the electrocardiograms discussed in the text. The third column gives the month of pregnancy in which the electrocardiogram was taken.

+ = upright P, R and T or a downward Q and S.
Blank = absent or iso-electric waves as indicated.
- = inverted waves.
± = diphasic waves.
θ = low, indefinitely shown or variable (slightly up, iso-electric, or slightly inverted) waves.

SUMMARY

A large Q_3 as defined by Pardee was found in seventeen of the 342 pregnant women. This is slightly less than 5 per cent. Ninety-eight of these women had organic heart disease or signs which justified a diagnosis of possible organic heart disease. Only three of these cases had large Q_3—slightly more than 3 per cent. Two hundred and forty-four of the women had no organic heart disease. Fourteen of these had large Q_3 (5.7 per cent).

The anginal syndrome was not present in any of this series, nor have we ever found it in a pregnant woman.

A large Q_3 may occur transiently, apparently modified by phases of respiration. We found nine such cases in this series.

A large Q_3 is frequently associated in this series with inverted T_3 and low or inverted P_3. These findings are characteristic of transverse position of the heart according to evidence from the literature.

The comparatively frequent occurrence of large Q_3 during pregnancy in patients with normal hearts, as contrasted with its reported rare occurrence in series of patients with normal hearts where pregnancy was not mentioned and probably was rarely present, suggests that a large Q_3 may be related to a transverse position of the heart such as occurs during pregnancy. In our opinion, therefore, a large Q_3 is not reliable as a sign of heart disease.

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ELECTROCARDIOGRAPHIC AND BLOOD PRESSURE CHANGES IN EXPERIMENTAL PERICARDIAL EFFUSION AND OCCLUSION OF THE VENAE CAVAE*

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CHANGES in the ST-segment of the electrocardiogram have been studied since 1909, when Eppinger and Rothberger[1] observed such changes in dogs following the injection of silver nitrate into the heart muscle. Their work was confirmed by others. In 1918 Smith[2] produced ST changes in dogs by ligation of the coronary arteries, and in 1919 Herrick[3] described such changes in clinical cases of coronary occlusion. A large mass of literature has accumulated with regard to these changes, and it is generally agreed that marked changes in the ST-segment are particularly frequent when there are infarctions near the apex. Changes in the ST-segment have been observed also in pneumonia,[4] in rheumatic fever,[5] after the use of digitalis, and, combined with changes in QRS, in bundle-branch block.

In 1929 Porte and Pardee[6] reported ST changes in patients with pericarditis. They did not consider specifically the question of pericardial effusion, but at least one of their patients had an excess of fluid in the pericardium as shown by the postmortem examination. Scott, Feil and Katz[7] reported the occurrence of marked ST changes in patients with pericardial effusion, notably one with an aneurysm which had ruptured into the pericardium and without active inflammatory changes or coronary disease. The same group of workers[8] reported at the same time a series of experiments on dogs in which they found elevation and convexity of the ST-segment, inversion of the T-wave, and shortening of the ST interval following the injection of fluid into the pericardium at various pressures. Foulger and Foulger[9] have confirmed these findings. We have failed to find in the literature any previous description of ST changes in pericardial effusions, although in several reports a casual mention of reduced QRS amplitude was encountered. Padilla and Cossio[10] have since reported changes in two patients, and Harvey and Scott[11] in one, similar to those reported by Scott, Feil and Katz.

The occurrence of ST changes similar to those of coronary disease in other conditions appears to justify experimental study with a view to learning the mechanism of the change.

EXPERIMENTAL OBSERVATIONS IN PERICARDIAL EFFUSION

The first portion of this report is concerned with a series of thirty experiments on nineteen dogs involving pericardial effusion obtained artificially

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by a method similar to that used by Katz, Feil and Scott. The pericardial pressure was recorded on a smoked drum by means of a mercury manometer. Tracings were made simultaneously of the pressure in the carotid artery with another mercury manometer. Electrocardiographic tracings were made by the three leads customary in the human electrocardiogram. In a few experiments the chest was allowed to remain open, and artificial respiration was maintained throughout the experiment; this did not appear to affect the results.

Elevation of the pericardial pressure produced uniformly a diminution of the carotid pressure. Our curves with regard to this change are similar to those previously reported by Williamson and Ets[12] and studied in greater detail by Foulger and Foulger.[9] Pericardial pressures of 4 to 6 mm. mercury produced little or no change in systemic arterial pressure, and additional pericardial pressure caused a fall of systemic blood pressure in an increasing degree. In eighteen experiments in which the arterial pressure was allowed to fall to 30 mm. mercury or less with gradually increasing pericardial pressure, the pressure required to produce such a fall varied from 11 mm. to 28 mm., averaging 17 mm.

The pressures in the right auricle were followed in four dogs by means of a manometer filled with normal saline connected with a catheter inserted through the external jugular vein into the auricle. In two it was consistently a little less than the pericardial pressure, and in two it was a little greater. In all cases it rose as the pericardial pressure rose, and there was no change in the relationship of the auricular and pericardial pressures when the arterial pressure fell rapidly.

In the electrocardiograms diminution of amplitude of QRS as the pericardial pressure was increased was observed in twenty-seven of thirty experiments. In three it was the only change noticed. With sufficient pericardial pressure to cause the arterial pressure to fall to less than 25 mm. and to abolish pulsations in the carotid cannula QRS was usually about one-third its normal height.

The most striking changes were in the ST-segment and the T-wave. In twenty-seven of thirty experiments these changes were present. They consisted of one or more of the following phenomena: deep, sharp inversion of the T-wave in all leads; elevation of the origin of the ST-segment; depression of the origin of the ST-segment; and marked convexity of the curve following QRS with a peak nearer S than the normal T-wave. Elevation of the take-off occurred twenty-four times. It was accompanied twenty-one times by both a sharply inverted T-wave and a broad upward convexity, and three times by a broad convex peak alone. In the experiments in which both convexity of ST and inversion of T were found, the inversion of T occurred first and the inverted peak was gradually effaced, partly or wholly, as the elevation and convexity of the preceding portion of the curve increased. Except for the fact that T was occasionally inverted in Lead I while still upright in Leads II and III, changes were always in

the same direction in all leads. Depression of the ST origin, with a plateau below the isoelectric line and with a sharply inverted T-wave, was seen in two dogs. In one experiment inversion of the T-wave with no change other than diminution of the amplitude of QRS was seen. A typical example of ST and T changes is shown in Fig. 1 *A*. The frequency of the types of change is summarized in Table I.

TABLE I.

OCCURRENCE OF CHANGES IN PERICARDIAL EFFUSION

EXPERIMENT NO.	ELEVATION OF ST	DEPRESSION OF ST	INVERSION OF T	CONVEXITY OF ST	DIMINUTION OF QRS AMPLITUDE	REMARKS
19	+		+	+	+	
20	+		+	+	+	
21	+		+	+		
22 A	+		+	+	+	
22 B		+	+			
23 A	+		+	+	+	
23 B	+			+	+	
23 C	+		+	+	+	
26	+		+	+	+	
37					+	Pressure raised to 20 mm.
41 A	+		+	+	+	
41 B	+		+	+	+	
42 A			+		+	
42 B	+		+	+	+	
43	+			+	+	
44	+		+	+	+	
47					+	Pressure raised to 6 mm.
62	+		+	+	+	
63	+		+	+	+	
64	+		+	+	+	
65		+	+	+	+	
66	+		+	+	+	
80 A					+	Pressure raised to 16 mm.
80 B	+			+	+	
81 B	+		+	+	+	
81 C	+		+	+	+	
82 A	+		+	+	+	
82 B	+		+	+	+	
82 C	+		+	+	+	
111	+		+	+		

In one of the three dogs in which T or ST changes were not observed the pressure was not increased above 6 mm. mercury. In only two did these changes fail to appear at a pressure of 16 mm. or more, and in only four dogs did they fail to appear at 8 mm. pericardial pressure.

Release of the pericardial pressure was followed immediately in all but three dogs by a recovery of the systemic blood pressure. It frequently rose above its previous level for a time. The amplitude of the QRS complexes was also increased immediately, and the cardiac rate was slowed for a few

minutes. The changes in T and ST showed striking variations in behavior. In twelve of the twenty-seven experiments in which such changes had occurred, the deviation of ST was greater for a time after the release of the pressure than before. In three of the twelve, changes were progressively greater until the death of the dog in spite of the fact that the pressure in the pericardial cavity had been released and that the systemic blood pressure was also improved for several minutes. In one the time of maximum change was not recorded; in eight the greatest height of the convexity of ST was found from the first to the fifth minute after the pericardial pressure had been released. After the fifth minute all these nine showed changes approaching the normal. In fifteen experiments the first tracing taken after the release of the pericardial pressure, in each case within two minutes and usually sooner, showed that the return of the curve to normal had already begun. There was no relation that we could discover between the height of the pericardial pressure or the duration of the pressure and the behavior of the curve following release.

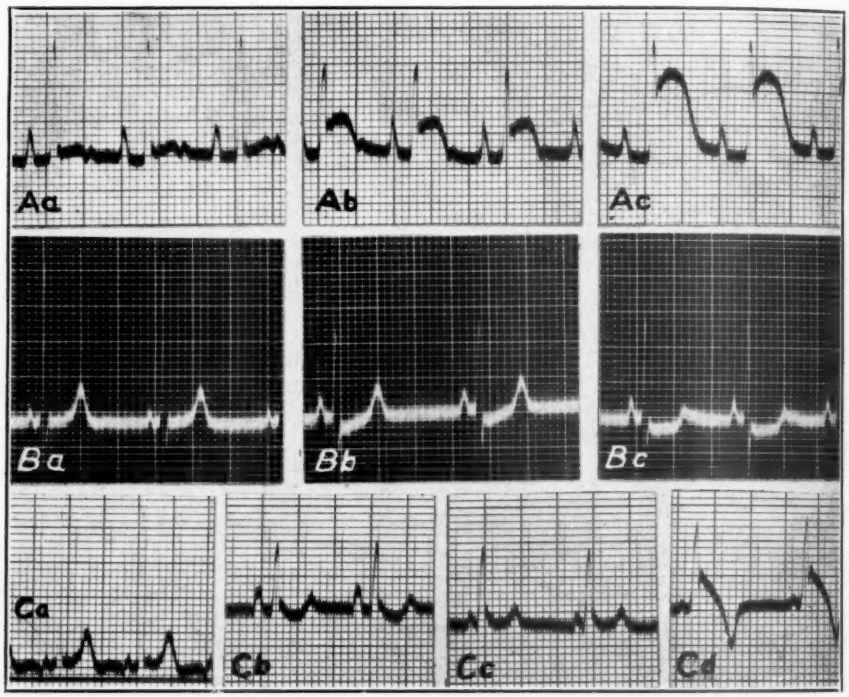

Fig. 1.—Electrocardiograms from typical experiments. All tracings are from Lead II.
A, Dog with pericardial effusion: Aa, control (pericardial cannula in place); Ab, maximum change during the effusion; Ac, maximum change after the effusion.
B, Dog with venae cavae ligated: Ba, control (ligatures in place but not tightened); Bb, maximum change during ligation of cavae; Bc, maximum change after ligation of cavae.
C, Dog on which both experiments were performed: Ca, control (cannula and ligatures in place); Cb, maximum change during ligation of cavae; Cc, recovery; Cd, maximum change during pericardial effusion.

In three dogs the experiments were performed repeatedly with the animal lying alternately on the back and on the belly. The curves were the same regardless of the change in position.

The electrocardiographic tracings taken to control the operative procedures showed changes in the ST-segment in two dogs. There were in one case slight elevation and slight convexity of the ST-segment during the period of pneumothorax and a normal tracing after the chest had been closed. The other is illustrated in Fig. 1 *A*. The amplitude of QRS following the operative procedures averaged 87 per cent of its height before the chest was opened. The changes were insignificant in comparison with those obtained by increasing the pressure in the pericardium.

In considering the mechanism by which changes in the electrocardiogram with pericardial effusions are produced, at least five possibilities present themselves. These are: (1) resistance offered to venous return, either to the right or to the left side of the heart with consequent lowering of the efficiency of the coronary circulation; (2) direct pressure on the cardiac arteries or veins or on the cardiac muscle; (3) chemical action of the normal salt solution used; (4) interference with the cardiac innervation; and (5) changes in temperature. Of these we regard the first two as of most importance for further consideration. The fact that recovery occurred with the heart still bathed in the solution used for the effusion but retained in the stretched pericardium at zero pressure speaks against chemical changes. The fact that the final part of the ventricular complex is the part affected would suggest that the extrinsic cardiac nerves were not the seat of the most important changes. Changes in temperature were undoubtedly present in spite of the fact that the fluid used for effusion was warmed to body temperature, but particularly in the animals in which the chest was left open during the experiment the temperature changes must have been as great during control periods and during periods of low pericardial pressure as during the period in which the pressure was raised sufficiently to result in electrocardiographic changes.

EXPERIMENTAL OBSERVATIONS ON OCCLUSION OF THE GREAT VESSELS

To determine whether or not interference with venous return to the heart was the important factor in producing changes, experiments were devised of two general types: first, occlusion of the great vessels to see whether such changes were produced thereby in the absence of pericardial effusion; and second, supplying fluid to the heart in the presence of a pericardial effusion to see if the changes were prevented.

In the great vessel occlusion experiments the dog was anesthetized with sodium barbital and artificial respiration established. The chest was opened just to the right of the sternum and the azygos vein was ligated near its termination. Ligatures were then passed about the superior vena cava and the inferior vena cava and the ends brought out through glass tubes so that the vessels could be occluded and released at will. In some of

the experiments the pericardial sac was removed and a ligature passed in a similar fashion about the pulmonary artery at its origin. With a few exceptions in which longer periods were used, constriction of the vessels was for two minutes in each experiment, as the animal frequently failed to survive the longer periods.

In thirty-three experiments on nineteen dogs involving occlusion of the inferior and superior cavae alone the blood pressure curves resembled those of the pericardial effusion experiments. The blood pressure fell somewhat more rapidly to 10 to 20 mm. mercury, and when the vessels were released it rose immediately, usually above the previous level for a few minutes. The rise in the blood pressure was regularly accompanied by slowing of the rate.

The electrocardiographic changes were chiefly in the T-wave and in the ST-segment. The degree was much less than that noted in pericardial effusion. In no case did the changes resemble the typical cove-plane curve seen in the pericardial effusion experiments. In each of the nineteen dogs there was a slight slurring of the origin of ST with the first experiment and this usually persisted. In eleven experiments there was no other change in the ST-segment. In four experiments there was a slight elevation, and in eighteen there was a definite depression of the ST at some time during the first two minutes after the release of the vessels. These changes occurred seventeen times before the veins were released but in each case became more marked during the first or second minute after release. Inversion of the T-wave occurred four times in thirty-three experiments. T was usually more positive after the release of the vessels and frequently reached heights of 10 or 12 mm. in Leads II and III. Changes were always in the same direction in all three leads. A typical series of curves is illustrated in Fig. 1 *B*.

OCCLUSION OF THE PULMONARY ARTERY

Inasmuch as the pericardial effusion pressures could conceivably affect the venous return both to the left and to the right sides of the heart, it was considered desirable to observe the effects of occlusion of the pulmonary veins in order to eliminate circulation of blood through the coronary and pulmonary circuits. As this offered very great technical difficulties, it was decided to occlude the pulmonary circuit on the arterial side, thereby accomplishing what would appear to be a mechanically similar result. Seven experiments were performed on five dogs in which the great veins and the pulmonary artery were occluded simultaneously for two minutes. Seven experiments on the same five dogs were performed in which the venae cavae were occluded alone for a similar length of time. The order in which the two kinds of experiments were performed was varied without any change in the results. In each of the experiments of this series, when the venae cavae were occluded alone, there was a slight depression of the ST-segment which became more marked when the vessels were released. The maximum deviation from the isoelectric line averaged 2.1 mm. and occurred uni-

formly during the first minute after release. When the pulmonary artery was ligated also, the changes were exactly the same, but of greater degree; the maximum deviation of ST averaged 3.0 mm. and occurred during the first minute after release in six experiments and during the second minute in one.

In five dogs both artificial pericardial effusion and occlusion of the veins were performed. With pericardial effusion both marked elevation of ST and inversion of T occurred in four and inversion of T with a convex ST approximately on the base line in the fifth. With occlusion of the veins the only marked change was increased height of the T-wave in four. The ST-segment deviated slightly upward in two and downward in two and was unchanged in one. The different types of curve obtained in the same dog are illustrated in Fig. 1 *C*.

In seven experiments the pericardial effusion was produced in the customary fashion and the ST changes described above were obtained. Following a recovery period the experiment was repeated, but at the same time physiological solution of sodium chloride was allowed to flow into the right auricle through a catheter inserted into the external jugular vein. The rate of flow was from 100 to 200 c.c. a minute. In these experiments the blood pressure fell slightly, but much less than when no infusion was given. The electrocardiographic changes were equally great in two, more marked in two, and less in three than in the ordinary pericardial effusion experiment. In none were ST and T changes prevented.

In four experiments a similar infusion was given into the left auricle through a special cannula which was inserted into the auricular appendage through a hole in the pericardium which was made water-tight by a purse string and nut about the cannula. In all of this series inverted T-waves were produced, and in three animals there was an elevation of the ST-segment. The electrocardiographic changes were the same in each animal with and without the infusion of fluid into the auricle, although the fall in blood pressure was less when the infusion was given simultaneously with the pericardial effusion.

It is evident from these experiments that elevation of the ST-segment of the electrocardiogram of the dog in the presence of pericardial effusion is not simply a function of the interference with venous return to the right side or to both sides of the heart. Interference with the venous return alone appears to have little effect on the ST-segment, but tends to produce changes in the opposite direction to those seen in pericardial effusions. Sudden filling of the heart, as when the occluded vessels are released, produces changes opposite in direction to those seen in pericardial effusion. Katz and Wallace[13] have produced evidence to indicate that fall in blood pressure contributes to the mechanism of ST changes in coronary occlusion, and while the general embarrassment of circulation may be a contributory factor here, we believe that it is necessary to assume some local action also, presumably compression of the cardiac muscle or of its vessels.

SUMMARY

The electrocardiographic and blood pressure changes previously reported in the presence of artificial pericardial effusions have been confirmed with some additional detail, particularly concerning the recovery period. Change in position of the animal does not alter the extent or direction of the observed changes. Simultaneous rapid infusion of normal saline solution into the right or left auricle modifies the blood pressure changes, but not the electrocardiographic changes. Transient occlusion of the venae cavae or of the cavae and the pulmonary artery causes a comparable drop in systemic blood pressure, but does not reproduce the electrocardiographic changes of artificial pericardial effusion, and tends to produce changes less in degree and opposite in direction. This difference holds whether the experiments are performed on the same or on different animals. Some possible mechanisms by which pericardial effusion might produce electrocardiographic change are discussed and interference with venous return, chemical changes, and temperature changes eliminated from consideration as the primary mechanism. The effect of direct pressure on the myocardium, on the coronary vessels, and on the Thebesian vessels remains as an important possibility.

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A SIMPLE METHOD FOR GRAPHIC DESCRIPTION OF CARDIAC AUSCULTATORY SIGNS*

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PHYSICIANS who are in the habit of recording their clinical observations are familiar with the sense of lack of completeness which they experience in describing cardiac auscultatory signs. One factor which contributes to this feeling of dissatisfaction is that in writing the record after the entire physical examination has been completed, there is an appreciable degree of uncertainty as to whether one's memory of the signs at various points over the precordium is exact. A second factor is that in order to describe the signs heard at all points, the report must be rather long, and one rarely escapes the feeling of tediousness both in writing and in reading it. Thus the record, if complete, is verbose, and if brief, is incomplete. By using the graphic method described below the memory factor is eliminated because the record is made while listening; and the signs can be accurately described without the use of any words in most instances, and only an occasional adjective to describe some peculiar quality of a sound or murmur in some cases.

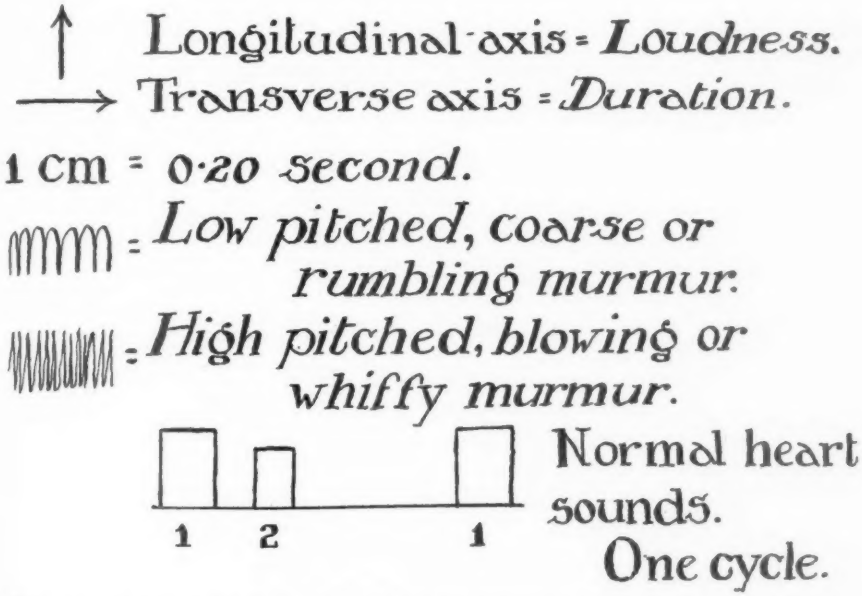

Fig. 1.—The code of symbols and rules for the graphic description of cardiac sounds and murmurs.

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The essential features of a heart sound may be expressed in terms of its relative loudness and duration; thus a loud, short sound has a sharp, snapping quality and a less loud, longer sound has a duller quality. By representing loudness in terms of the vertical axis and duration by the horizontal axis a rectangular figure describing the heart sound is drawn. It is obviously necessary to adopt some general rules for guidance in determining first, the size of the rectangles and second, the length of the spaces between them which denote time intervals. As the standard size of average

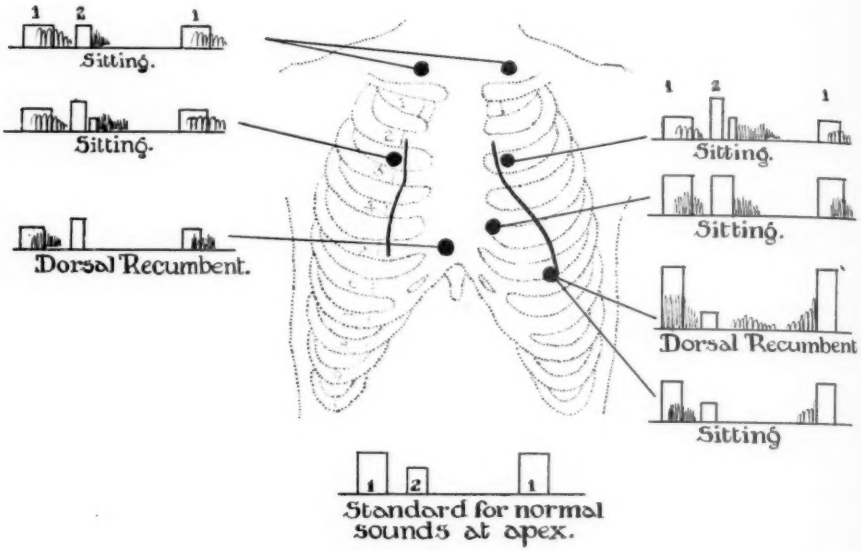

Fig. 2.—The auscultatory signs observed in a case of rheumatic heart disease with aortic stenosis and insufficiency and mitral stenosis and insufficiency. The practical value of the graphic method, its accuracy and effectiveness as a time-saving procedure are well illustrated by comparing the above record, the original of which was made as the observer was listening over the heart, with the following verbal description.

At the apex: the first sound is loud and sharp and accompanied by a blowing systolic murmur which continues almost up to the second sound; both the sound and the murmur are louder in the dorsal recumbent than in the sitting posture; the second sound is rather faint. In the sitting posture a short presystolic, rough crescendo murmur is heard. In the dorsal recumbent posture, a rumbling mid-diastolic decrescendo murmur and loud, rough, presystolic murmur are heard; the latter is longer than in the sitting posture. At the left border of sternum, in the fourth space, the first and second sounds are moderately loud, the second is sharper than the first; a late systolic blowing murmur accompanies and follows the first sound, and a blowing diastolic murmur of about equal loudness follows the second sound without any interval between the end of the sound and the beginning of the murmur. At the pulmonic area the first sound is less loud than at the apex and is accompanied by a moderately loud, somewhat late, rough systolic murmur; the second is duplicated, the first half being louder than the second half and also louder than the first sound; a blowing decrescendo diastolic follows immediately after the second half of the second sound. At the aortic area, the first sound and systolic murmur are similar but somewhat louder than at pulmonic area; the second is duplicated but less loud than at pulmonic area, and the diastolic murmur seems similar in all respects. In the neck region, above the clavicle, the sounds and murmurs are about as at the aortic area, except that the second sound is not duplicated. At the tricuspid area, both sounds are less loud than anywhere else over precordium, and there is only a relatively short, late blowing systolic murmur.

normal sounds, 10 mm. (vertical) by 7 mm. (horizontal), for the first sound, and 7 mm. by 5 mm. for the second, are convenient and suitable. The time is expressed in terms of 1 cm. for 0.20 second. By describing the

first and second sounds of one cycle and the first sound of the next, one indicates the nature of the heart rate, and the length of systolic and diastolic periods is clearly portrayed. If the rhythm is normal, only one cardiac cycle need be described (Fig. 1); variations in rhythm may be described by recording a series of sounds in the order in which they are heard. The relative loudness and duration of the sounds are expressed by varying the size and shape of rectangles. Holding the stethoscope with one hand the graphic notes are made with the other, while listening.

The point at which the signs are observed can be accurately recorded with the aid of a simple diagram of the heart. I have tried using the

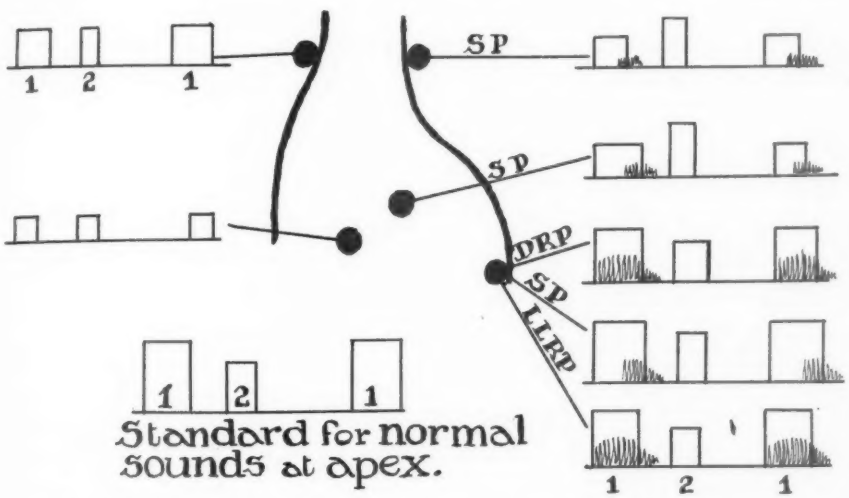

Fig. 3.—Using a simple diagram of the heart, without an outline of the thorax, the points at which the stethoscope is applied may be satisfactorily indicated. The relative loudness of the sounds, the loudness, duration and time relations of the blowing systolic murmur at various points over the precordium are portrayed. S.P. = sitting posture; D.R.P. = dorsal recumbent posture. L.L.R.P. = left lateral recumbent posture.

orthodiagraphic chart of the heart in its actual size for recording the signs graphically at the very points where the stethoscope was applied, but have found it less simple and convenient than the method shown in Figs. 2 and 3, which requires only the ordinary notepaper, preferably with an outline of the thorax stamped on it.

The essential features of a heart murmur are: first, its time relations to the heart sounds; second, its pitch; third, its loudness; fourth, its duration; and last, the point, or points, at which it is heard. The pattern of a single cardiac cycle (Fig. 2) offers a convenient plan for recording accurately the portion of the cycle during which a murmur is heard; thus its time relations to the sounds and its duration are readily indicated. The pitch of a murmur is either high or low, depending on the dominant vibration frequency of its sound waves. Thus low-pitched murmurs may be described by a series of rather widely separated vertical lines joined by

curves, forming a serrated border (Fig. 1) to indicate the dominance of low vibration frequencies. In the presence of a sufficiently loud low-pitched murmur a thrill is palpable; the serrated border of the diagram representing the low-pitched murmur suggests the tactile sensation of a thrill. High-pitched murmurs are represented by closely placed vertical lines to indicate higher vibration frequency. The loudness of the murmur is conveniently described by varying the vertical length of the lines, the description of the loudness of the heart sounds being used as a standard for comparison. The points at which the murmur is heard are readily indicated by referring to a diagram of the heart as in Fig. 2 or Fig. 3.

AORTIC ANEURYSM WITH HUGE SECONDARY ANEURYSM OF THE CHEST WALL. REPORT OF A CASE

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A THIN colored laborer, thirty-two years of age, entered Cook County Hospital, February 5, 1932, complaining of substernal "soreness," pain in the left shoulder and chest, productive cough, loss of 15 pounds in weight, and dyspnea on slight exertion. The initial symptom, substernal discomfort, had been present for one year. He had had gonorrhea twice and a chancre at the age of twenty years, for which he received forty-eight mercury inunctions. He had drunk one-half pint of whiskey daily for ten years. The family history was not remarkable.

On the first examination there was a small pulsating mass at the right sternoclavicular articulation over which a systolic thrill could be palpated. There was extensive widening of mediastinal dullness (15 cm.) The heart was enlarged slightly to the left (11 cm. from the midsternal line). A systolic murmur at the base and booming aortic second sound also were present. Other findings were: Hyperresonance over the apex of the right lung anteriorly and hyporesonance over the same portion posteriorly; decrease in Kronig's isthmus on the left side; extension of hilar dullness laterally 6 cm. from the spine on the right side; enlarged, tender prostate; carious teeth and slightly enlarged lymph nodes in the right supraclavicular fossa. The blood pressure of the right arm was 100/74, of the left arm 110/84, pulse rate 104, temperature 98.6 degrees. Wassermann tests of blood serum and spinal fluid were negative. The erythrocyte count was 4,200,000, hemoglobin 78 per cent, and leucocytes 10,500. The urinalysis was negative except for an occasional hyalin cast. The electrocardiogram showed a sinus mechanism, normal conduction time and a prominent Q-wave in Leads II and III. X-ray and fluoroscopic examinations revealed a large aneurysm involving the aorta, with marked opacity in the middle half of the right lung.

He was given bismuth salicylate intramuscularly for one month. March 14 he left the hospital without permission.

The patient returned June 6, 1932, complaining of shortness of breath, numbness of the right hand and arm and a large swelling of the right chest.

Examination now showed a large tender mass, extending from the right infraclavicular area to about the third intercostal space, which had an expansile pulsation synchronous with the heart beat. The blood pressure

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in the right arm was 110/90 and in the left arm 120/90. There were no other changes in the physical findings. The erythrocyte count had dropped to 3,400,000 and the hemoglobin to 60 per cent. The electrocardiogram was not changed. The condition of the patient rapidly became worse. He experienced a moderate amount of pain which was readily relieved by morphine. The size of the mass increased rapidly so that on June 18 it measured 12 by 20 cm. and was 10 cm. in height. It became more tender, and three days before death blood began to ooze through the skin. An electrocardiogram made on this date showed a marked decrease in voltage in all leads, especially the first. June 24 the patient fell out of bed, with no demonstrable bad effects. He became more and more dyspneic and died June 26.

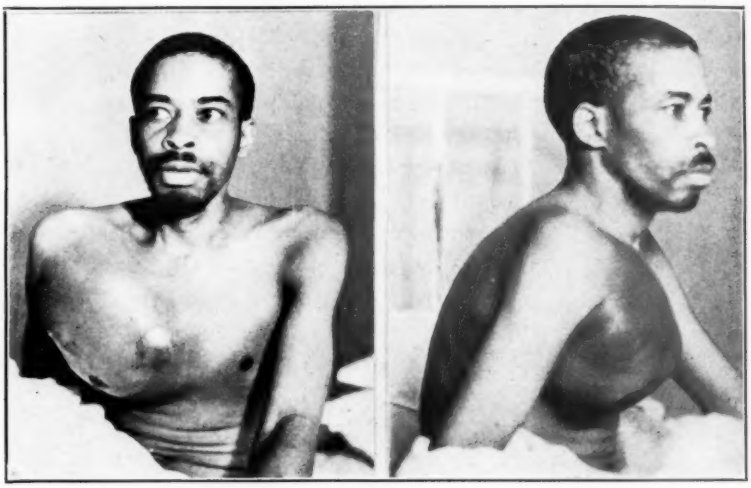

Fig. 1. Fig. 2.

Fig. 1.—Front view of patient taken June 20.
Fig. 2.—Side view of patient. Same date as in Fig. 1.

A necropsy showed a bulging mass of the right chest which measured 15 by 24 by 25 cm. The veins of the chest were dilated, and the skin overlying the swelling was thin and hemorrhagic. The mass was a huge sac-like structure formed by the muscles and fascia of the chest, and filled with laminated blood clot. The sac communicated with a similar cavity in the right pleural cavity by a tract between the second and third ribs. These ribs were separated widely and partially eroded. The sac in the pleural cavity was continuous with a large fusiform aneurysm involving the entire arch of the aorta. The heart was moderately enlarged. The myocardium was purple gray in color and friable. Immediately above the aortic valve was a fusiform dilatation of the aorta involving the entire arch, forming an aneurysm about 14 cm. in diameter filled with laminated

blood clot. The entire intima of the aorta was wrinkled and puckered with scars. The body of the fourth dorsal vertebra was eroded.

The anatomical diagnosis was:

Fusiform aneurysm of the arch of the aorta, eroding through the right chest wall with secondary aneurysm formed by the chest wall; syphilitic aortitis; fatty infiltration of the liver; parenchymatous degeneration of

Fig. 3.—X-ray picture of chest taken June 7.

the myocardium; chronic tumor of the spleen; decreased lipoid content of the adrenals and marked passive congestion of the kidneys.

COMMENT

A report is made of a fusiform aneurysm of the aorta with an enormous secondary aneurysm of the chest wall.

Despite the size and character of the aneurysm, rupture did not occur because of the laminated clot within the sac. Death was the result of cardiac exhaustion.

Department of Clinical Reports

THE REMOVAL OF A LARGE NEEDLE FROM THE HEART WITH ELECTROCARDIOGRAPHIC CHANGES IN RHYTHM DURING OPERATION*

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THE removal of foreign bodies from various situations in the heart is recorded from time to time. These have included needles, nails and particularly during the war, bullets, and other foreign bodies. Of the cases reported, the needle has not infrequently been mentioned and, when penetrating deeply, has, in many cases, been followed by death. Hinton[1] reported one and quotes Meyer-Pantin[2] who collected twelve such cases.

Apart from those cases in which death is an early event, it is remarkable how some patients will tolerate a large foreign body apparently for a considerable length of time. Occasionally a foreign body, corroded and friable, has been found incidentally at autopsy, and its appearance has suggested that it has been retained for a number of years.

The patients who survive its entry generally develop symptoms which gradually increase in severity. Intense precordial pain and dyspnea have been frequently noted, and in one case reported[3] irregularity of the pulse and tachycardia supervened.

CASE REPORT

A case which came to our attention was that of a girl, twenty-two years of age, who was referred to this hospital in the surgical service of Dr. F. A. C. Scrimger. Her complaints were those of severe pain over the precordium, radiating over the front of the chest; weakness, and dyspnea on exertion.

Her history was that five months previously, while employed as a domestic, she fell to the floor while doing her housework. In falling, a needle which she had stuck in the front of her dress, was driven into the wall of her left chest. It was, at the time, quite painful but she did not immediately seek medical advice. The needle apparently disappeared completely from sight and no attempt was made to recover it. During the ensuing weeks she became increasingly troubled with pain in the chest. It was described as sharp and severe, but never of a stabbing character. It gradually became persistent and was constantly present, day and night. At times it radiated across the front of the chest from a point of maximum intensity over the precordial region. It did not radiate down either arm, or to the back. It was not associated with faintness or loss of consciousness. The pain was greatly increased by movements of her arms and for sometime past she had been unable to work. Four weeks previous to admission the pain became so severe that she was completely in-

*From the McGill University Clinic, Royal Victoria Hospital. The surgical aspect of the case is being reported elsewhere by Dr. Scrimger.

capacitated and was forced to consult a physician. At this time she began to experience some difficulty in breathing, a condition which added greatly to her disability. An x-ray film disclosed a needle-like shadow within the cardiac area, and she was referred by Dr. A. V. Traynor of Kitchener, Ont., to the Royal Victoria Hospital.

Her personal history revealed that she was born in Ukrainia, that there had never been any cardiac symptoms prior to the present illness and that there was no history of previous illness.

The patient was well developed, and, except in the cardiovascular system, examination revealed nothing of importance. The pulse was regular; there was no evidence of arterial thickening, and the blood pressure was 130 mm. Hg systolic and

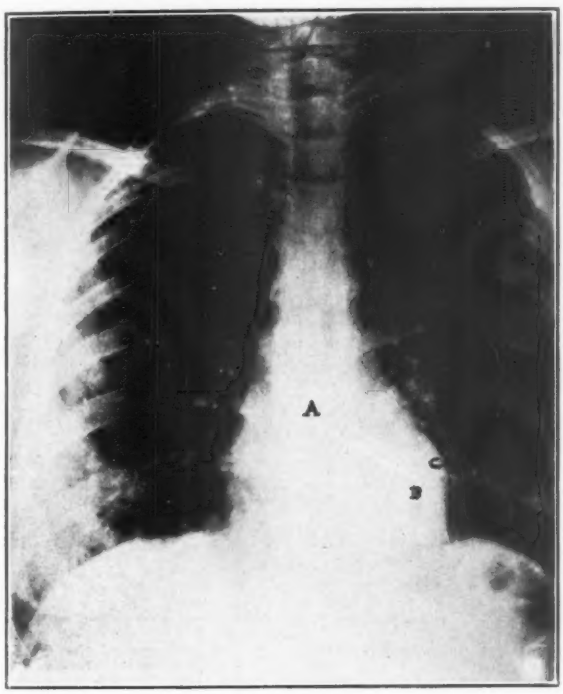

Fig. 1.—Needle 7 cm. in length lying within the heart. The point is at *B*. The pericardial adhesion is at *C*.

94 mm. Hg diastolic. There was no evidence of increase in venous pressure. The heart was slightly enlarged to the left. The sounds were regular, and of normal intensity. There were no murmurs present. There was no pericardial friction rub or evidence of increase in fluid in the pericardial cavity. The lungs were clear. The liver and spleen were not enlarged. There was no peripheral edema. The urine was normal. The leucocyte count was 6,400. The temperature was normal and remained so until operation.

A combined fluoroscopic and stereoscopic examination revealed a large needle lying within the cardiac shadow about midway between the sternum and vertebral column and pointing obliquely posterior. There was marked oscillation of the needle of about one inch with each cardiac contraction. The needle was judged to have penetrated the anterior surface of the left ventricle and, pointing posteriorly, to be lying within the cavity or myocardium of the left ventricle. Fig. 1 is an x-ray pic-

ture of the heart showing the position of the needle in an A-P view. The point of the needle, as later determined, is at *B*. The pericardial adhesion was at point *C*.

The electrocardiogram (Fig. 2) taken on admission shows a low voltage of the QRS deflections with an acutely negative T deflection in the second and third leads. This was taken as evidence of localized ventricular muscle damage. The electrocardiogram resembles that seen in coronary thrombosis of some duration.

The operation by Dr. Scrimger, reported in detail elsewhere, was as follows:

An incision was made from the level of the second rib in the midsternal line downward to the xiphoid and then across to the left parallel to the rib margins three inches beyond the tip of the xiphoid. The sternum was then chiselled through about its midpoint from the xiphoid to the level of the second rib. The chisel was then turned and the sternum cut through into the second rib and the cartilage of the second rib cut with the knife, thus making an osteoplastic flap which exposed the anterior

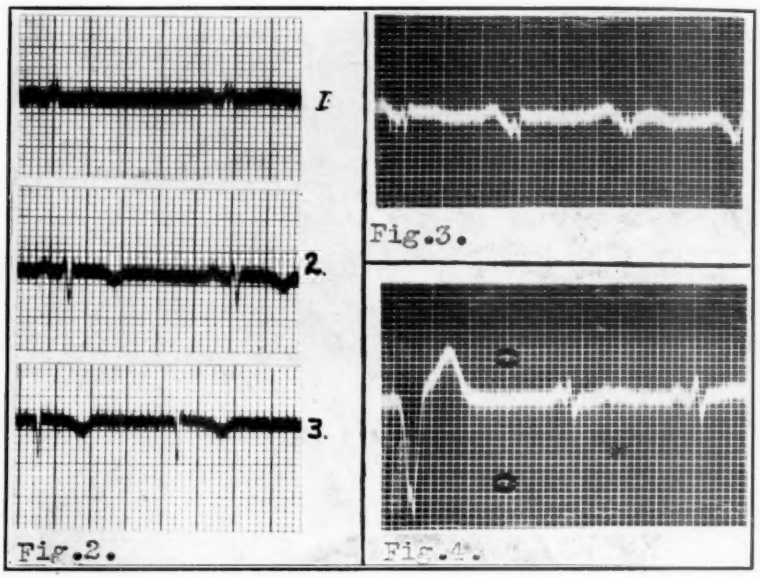

Fig. 2.—Tracing taken before operation. A low voltage of the QRS deflections and negative T deflections in the second and third leads may be observed.

Figs. 3 and 4.—A period of lowered voltage with occasional extrasystoles on inserting the hand into the pericardial cavity was followed by a change in the QRS deflections (Fig. 3). Fig. 4 follows shortly after with a return to the previous QRS formation. The hand of the operator was in the pericardial cavity with the palm on the posterior surface of the heart. (Lead II.)

mediastinum. The pleura was pushed away toward the left until a good exposure of the anterior mediastinum was obtained. The pericardium was then opened.

During chiselling of the sternum, no change in the electrocardiogram was observed. On opening the pericardial sac, there was a decrease in voltage of the QRS and T deflections.

A normal amount of pericardial fluid was found and the heart was exposed, beating regularly. The heart was covered with fat on the surface. On exploring the pericardium with the finger, no sign of the needle could be found. This manoeuver elicited left and right ventricular extrasystoles, which in turn were followed by a regular rhythm.

The only deformity was a band of rather firm, fibrous adhesions about three-fourths of an inch broad extending from the inferior surface of the left ventricle to

the pericardial wall. This was hooked with the finger and brought forward into view and cut.

This manipulation in the pericardial cavity was accompanied by a marked change in the electrocardiogram. A marked notching of the QRS deflections was observed, later followed by one left ventricular extrasystole and a return to normal deflections. (Figs. 3 and 4.)

The hand was introduced around the heart, feeling toward the base among the roots of the great vessels. This could only be carried on for a matter of a few minutes at a time and if prolonged resulted in marked pallor and disappearance of the pulse together with changes in the pupils, sometimes dilatation and sometimes contraction. After several such attempts, a portion of the needle was recognized as projecting from the posterior surface of the heart about three-fourths of an inch into the pericardial cavity.

At this point a prominent S-wave in the electrocardiogram was replaced by a prominent and notched R deflection which was followed by alternate right and left

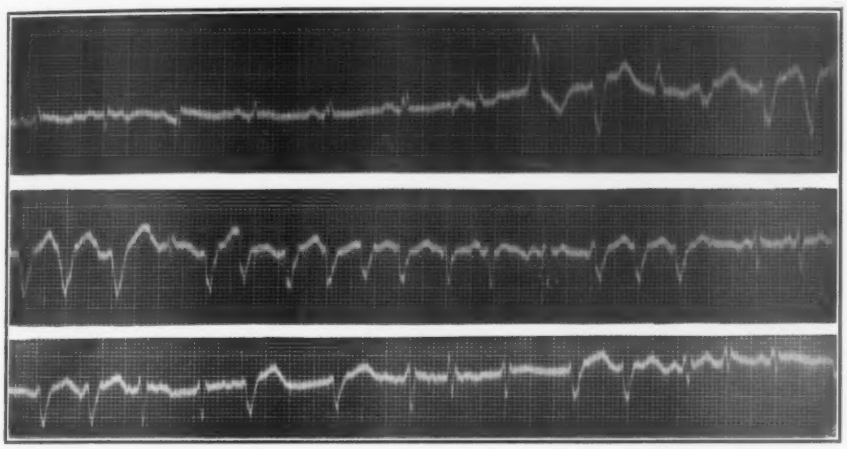

Fig. 5.—The tracing is a continuous one taken when the operator's hand was in contact with the needle. In the first part a change in form of the QRS deflections is seen followed by alternate right and left ventricular extrasystoles and a ventricular rhythm interrupted by an occasional supraventricular beat. In the last part a return to the normal is seen. The tracing is Lead II.

ventricular extrasystoles and then a ventricular rhythm interrupted by an occasional supraventricular beat. The heart then returned to a normal rhythm. (Fig. 5.)

This free portion of the needle was situated among the great vessels at the base of the heart. The needle in this situation was not free, but there was some soft tissue between the finger and the needle. After several attempts to feel it, it was recognized that the needle lay in an oblique position extending downward and to the left and lay mostly in the substance, or in the cavity of the left ventricle. As it seemed too dangerous to attempt to withdraw the needle by grasping the exposed portion, the thumb of the right hand was placed on the exposed portion of the needle posteriorly, and the heart being grasped between the fingers of the hand, the needle was thrust forward in the line of its axis until the point appeared through the anterior wall of the ventricle for about one-half an inch. The point of the needle corresponded fairly closely to the situation of the adhesions which had previously been released. At this point the pulse disappeared and the patient stopped breathing.

The appearance of occasional runs of ventricular tachycardia continued until the operator's hand was in contact with the needle and was attempting to dislodge it.

At this point there developed an irregular rhythm of right ventricular origin which changed to one of left ventricular origin. (Fig. 6.) This rhythm was irregular and seemed not far removed from ventricular fibrillation. This coincided with the disappearance of the pulse and cessation of respiration. The heart then returned to a normal rhythm.

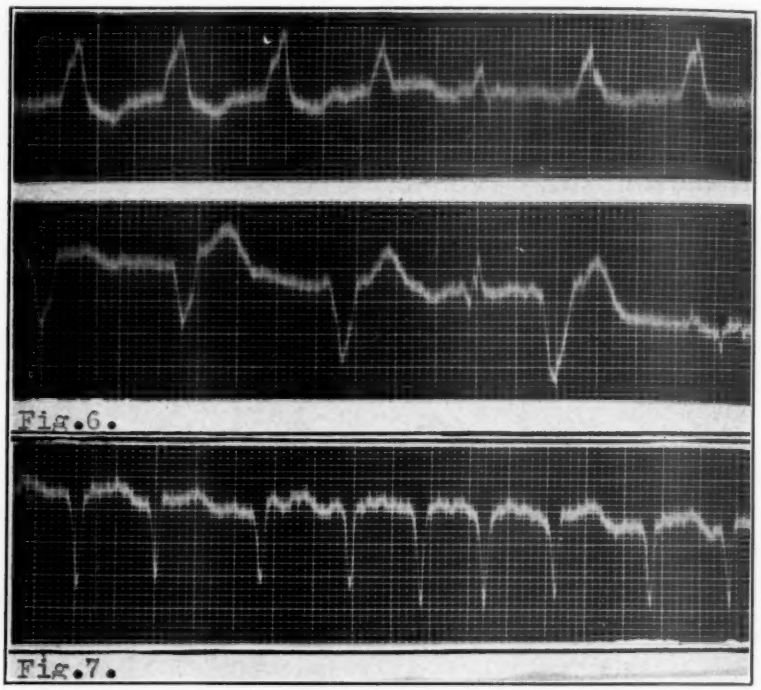

Fig. 6.—Portion of a continuous tracing taken when the operator was attempting to dislodge the needle. A rhythm of right ventricular origin changed to one of left ventricular origin. The average rate is 81 per minute. (Lead II.)

Fig. 7.—Ventricular tachycardia, rate 138 per minute. Taken when the operator was forcing the needle through the wall of the left ventricle. (Lead II.)

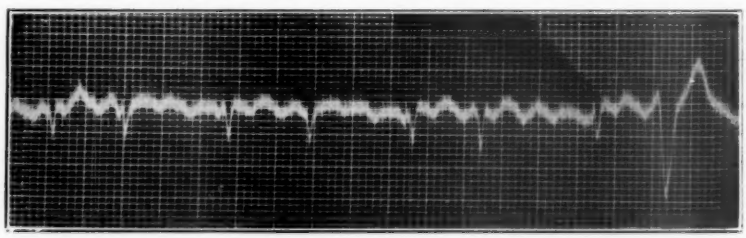

Fig. 8.—Lead II taken immediately following Fig. 7. Auricular flutter with left ventricular extrasystole. This was followed by short runs of ventricular tachycardia.

The heart, therefore, had to be released from the grasp of the hand. As soon as this was done, and this had to be repeated four or five times with the same result, the heart took up its rhythm again; the pulse re-appeared and the color improved. At no time, however, did the pulsation of the heart cease or the muscle lose its tone. On the third attempt, the portion of the needle which projected from the wall of the ventricle was grasped between the first and second fingers of the hand inside the pericardium and gradually withdrawn through the heart and removed.

Just prior to grasping the needle, the rhythm had again returned to normal, when on grasping the needle and forcing it through the heart (left ventricle) a continuous ventricular tachycardia, rate 138 per minute developed. The tachycardia was left ventricular in origin. (Fig. 7.) As the needle was removed this, in turn, was succeeded by an auricular flutter interrupted by an occasional left ventricular extrasystole. (Fig. 8.) The rhythm then returned to normal.

There was a small amount of bleeding into the pericardium, but nothing alarming. After waiting some time to allow the heart to recover its rhythm and the pulse and color to improve, the pericardium was closed with continuous suture. The sternum was then replaced and sutured into position. The wound was closed without any drainage. At no time was the pleura opened. The patient left the table in good condition, color satisfactory, pulse about 90 and blood pressure 120/70.

The electrocardiogram (Fig. 9) taken just before leaving the operating table showed a regular rhythm; rate 90 per minute. The voltage was somewhat lower than before operation. The needle removed was of the "darning needle" type and measured 7 cm. in length. It lay obliquely, postero-anteriorly, about three-fourths of an inch of the "head" protruding from the right auricle into the pericardial cavity posteriorly at the root of the great vessels. The body of the needle lay in the myocardium of the left ventricle, the "point" directed latterly. Whether a portion of the body of the needle lay within the cavity of the left ventricle, could not be accurately determined. The needle had blood crusts on the surface but showed no signs of corrosion. The needle after penetrating the chest wall had evidently penetrated the anterior wall of the right ventricle or auricle and had been pulled into the position described.

The operation was performed on June 17, 1932. The following day, June 18, the pulse averaged about 120 per minute. Temperature 99° F., blood pressure 110/80. The electrocardiogram (Fig. 10) showed an increase in the voltage of the QRS deflections and an elevation of the R-T interval in Leads I and II, a tracing resembling that of an acute coronary occlusion. She complained of severe pain in the region of the sternum and some respiratory distress. Three hundred cubic centimeters of a 20 per cent glucose saline solution was given intravenously.

On June 21 she was very restless, and the respirations had increased to 40 per minute. The temperature was 100° F. and the pulse was 120 per minute. The blood pressure was unchanged. There was a suggestion of a small amount of fluid in the pericardial cavity. At the base of the left lung there was a small area of consolidation similar to that frequently seen in acute pericarditis. The electrocardiogram showed the elevation of the R-T interval in Leads I and II slightly more marked. The possibility that this might be due to the pericardial effusion, though moderate, as suggested by Scott, Feil and Katz[4] was considered. It was thought more probable, however, that it was due to the recent damage to the ventricle on removing the needle.

During the next few days the blood pressure decreased slightly, averaging about 98/68. On June 27, the blood pressure was 102/65. Temperature 100.4°. The lungs were now clear. The electrocardiogram had changed (Fig. 11); the T deflection in Lead I showing an upward convexity, later becoming negative; it was diphasic in Lead II and isoelectric in Lead III. There was also some decrease in voltage of the QRS deflections.

On June 30 the temperature was normal and remained so. On July 2 she was up in a wheel chair, and on July 5 she was walking about the ward. On July 7 the electrocardiogram showed a negative T deflection in all leads together with a low voltage of the QRS deflections. (Fig. 12.) She was discharged from the hospital on July 8, free from all symptoms. Examination showed slight enlargement of the heart. There were no murmurs present.

She returned to the hospital for an electrocardiogram on July 20 (Fig. 13). The

T deflection was now upright in Lead I. On August 3 the T deflection had become upright in Leads I and II but remained negative in Lead III. This might be taken as evidence of improvement over the tracing taken before operation, (Fig. 2). In

Fig. 9.

Fig. 10.

Fig. 11.

Fig. 12.

Fig. 13.

Fig. 14.

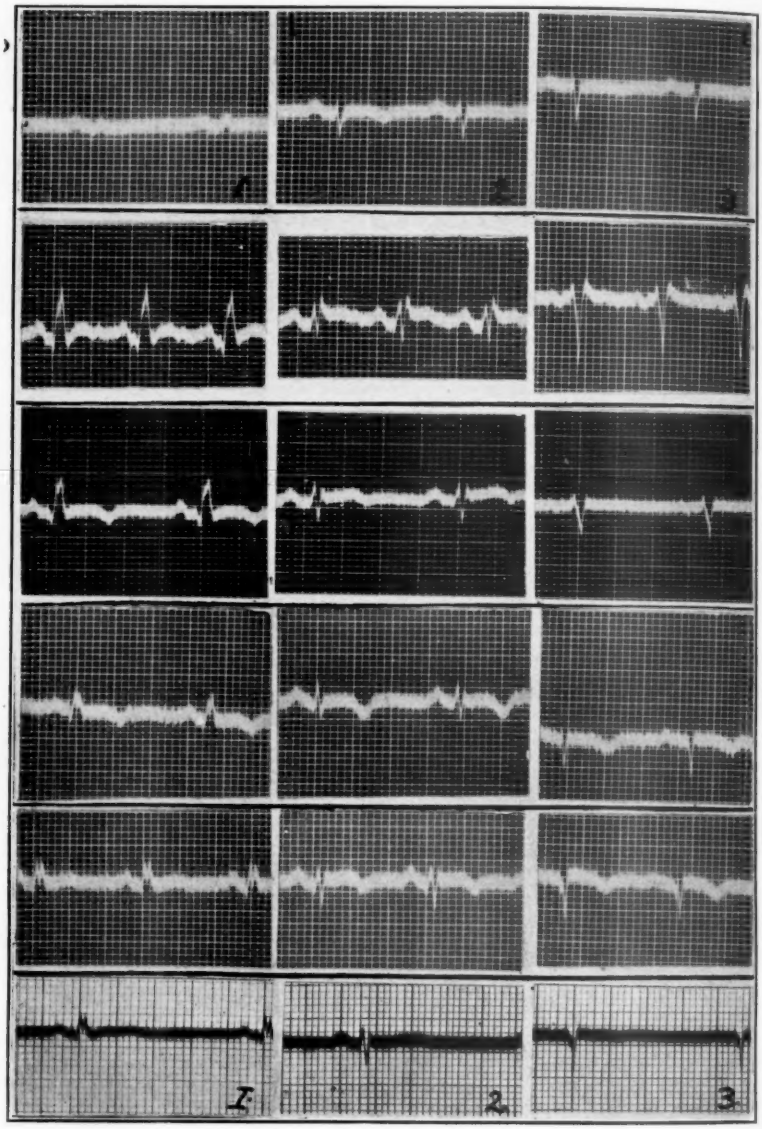

Fig. 9.—Electrocardiogram taken just before leaving the operating table. The voltage was somewhat lower than that before operation.

Figs. 10 to 14.—Progressive changes in the electrocardiogram taken at subsequent dates after the operation, which was performed June 17. Fig. 10, June 18; Fig. 11, June 27; Fig. 12, July 7; Fig. 13, July 20; Fig. 14, December 9.

the latter the T deflection in Lead I was of low voltage, and was acutely negative in Lead II. She returned for examination on December 9. In the interval she had been entirely free from symptoms and had returned to work. The electrocardiogram is shown in Fig. 14.

DISCUSSION

Extrasystoles have been produced in the human heart by stimulation of the ventricles.[5, 6] In our case these were readily produced on handling the heart with the needle in situ. Further handling, with the lifting of the heart in the pericardial sac, produced a lower voltage with notching and widening of the QRS deflections. This may be taken as evidence of conduction changes within the ventricles and may possibly be explained on the basis of a relative cardiac anoxemia. This factor, together with the stimulation of the ventricles on attempting to dislodge the needle, probably favored the development of the ventricular tachycardia. Davis,[7] who thinks that the normal functioning of the conduction system tends to prevent the development of a ventricular tachycardia, states that "disease or drugs that depress the conducting tissues tend to interfere with this normal control and permit the development of circus movements in the ventricles."

The changes in the electrocardiogram following the operation may be explained by the damage to the myocardium and smaller branches of the left coronary artery on removing the corroded needle. The closer approximation toward the normal, as seen in the last electrocardiogram, is probably due to healing after removal of the needle.

SUMMARY

A case is reported of a girl, twenty-two years of age, complaining of severe precardial pain and dyspnea, who had, for a period of five months, a darning needle, 7 cm. in length, lying mainly in the myocardium of the left ventricle.

Electrocardiograms taken during the operation for removal showed extrasystoles, ventricular tachycardia, an irregular ventricular rhythm and auricular flutter.

Successful removal and uneventful recovery with progressive changes in the electrocardiogram resembling that of acute coronary occlusion.

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Department of Reviews and Abstracts

Critical Review

THE EFFECT OF CALCIUM ON THE HEART

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IN RECENT years, the study of the inorganic constituents of the body has received more attention than ever before. Calcium research, in particular, has been profoundly stimulated by the discoveries of vitamin D and the parathyroid hormone. Of the multitude of calcium effects observed, one very important one is perhaps least well known, i. e., its effect on the heart. This effect has been investigated from four different angles: (1) by physiological experiments on isolated hearts and on living animals; (2) by electrocardiographic studies, following either spontaneous or induced changes in the blood calcium level; (3) by pharmacological experiments, conducted chiefly to analyze the similarity of calcium and digitalis effects; (4) by clinical observations, obtained by administering calcium to human subjects.

PHYSIOLOGICAL EXPERIMENTS

In the seventies of the last century, the school of the physiologist Ludwig undertook for the first time to investigate the underlying chemical conditions of the heart beat, and Merunoviez was able to show that isolated frogs' hearts could be kept beating normally in an aqueous extract of the ash of blood serum almost as long as in the serum itself. Ringer, in 1882, was the first to demonstrate that the amount and duration of cardiac contractions depend entirely on the relative quantity of the normal mineral constituents of the blood. Ringer's fluid, a mixture of sodium, potassium, and calcium salts, has long since become world famous. It was Ringer who recognized that the addition of a calcium salt to physiological salt solution was necessary for the maintenance of contractility. He also observed that, when an excess of calcium was present in the perfusing fluid, the contractions soon became very vigorous, and the diastolic relaxation diminished progressively until, finally, the heart was thrown into a state of tetanus.

Subsequent investigations were made on living animals and were directed largely toward an attempt to discover the individual influence of each of the elements in question. Jacques Loeb, in 1900, experimented with a hydromedusa, Gonionemus, which contracts rhythmically like a heart. He came to the conclusion that calcium and potassium were not in themselves necessary to maintain contractions, and that they served only to eliminate the toxic effects of a pure sodium chloride solution. It remained for Howell to prove that calcium, not sodium is the most important factor in the production of cardiac contractions. He pointed out that even when there was no trace of calcium in the bathing solution, there still were diffusible calcium salts in the heart muscle. For his own experiments, Howell used strips of ventricular muscle of the terrapin. Spontaneous contractions of the strips depended upon the presence in the tissue of dissociable compounds of both calcium and sodium. Sodium salts in the liquid surrounding the strips produced a relaxation. Calcium salts, on the contrary, caused a shortening through increase of tone which at times passed into permanent rigor.

Boehm, in 1913, thoroughly reinvestigated the whole subject of the rôle played by the different cations in maintaining the contractility of a frog's heart. He described the effect of calcium ions as:

1. Positively inotropic—prolongation of systole, tetanic contractions, and, as maximal effect, systolic standstill.
2. Negatively chronotropic—slowing of the rate.
3. Positively bathmotropic—shortening of the refractory phase.

Boehm noticed that the calcium or potassium concentration of the perfusing Ringer's fluid had to be increased to at least four or five times the usual concentration in order to get the prevailing influence of one of the two ions. This finding is worth emphasizing, particularly in regard to the human blood calcium level which we can never hope to raise to such a high degree.

Perfusion experiments on frogs' hearts performed by Arima supplemented the older experiments. He also found that if he perfused the hearts with a calcium-free Ringer's fluid, the contractions stopped soon, but they began again, spontaneously, after an interval of about one hour. This recovery was proof of Howell's contention that the heart muscle yielded stored calcium to the perfusing fluid. On analyzing that fluid, Arima now discovered calcium in it!

That calcium could be replaced to a certain extent by barium and strontium, had been shown by Ringer as early as 1886, and was confirmed later by Mines and by Jacques Loeb. Hoeber added cobalt, manganese, and nickel to the list of calcium substitutes. But Hoeber also demonstrated that with none of those cations could all the calcium effects be produced. The unique importance of calcium for maintaining the heart action remained definitely established.

The next step which subsequent investigators had to take concerned the site of attack of calcium in the heart. That the effect of calcium on the heart was not due to stimulation of any part of the central nervous system was borne out early by experiments of Rothberger and Winterberg. These authors perfused hearts of cats which were immobilized by injecting curare or by severing the medulla. Then they measured the cardiac output and rate before and after introduction of calcium chloride into the artificial circulation, and they found that the calcium salt produced a very considerable increase in the cardiac output. This was accompanied by moderate slowing of the heart rate. It is to be noted that the hearts were no longer under the control of the central nervous system, and that calcium chloride exerted its effect upon the heart itself. The problem was thus narrowed down to the question upon what structures within the heart calcium acted. In another series of experiments the same authors showed that calcium increased the irritability of the idioventricular centers. Large doses of calcium produced ventricular automatism immediately. The sinus and the atrioventricular nodes remained unaffected.

Later Fröhlich and Amsler demonstrated that calcium affected not only the idioventricular centers, but also the contractile elements of the ventricles. And a third site of attack was found by Pick in the conductive system. Large doses of calcium, he showed, produced definite blocking of the impulses between auricles and ventricles.

A fourth effect of calcium, however, the effect on the cardiac nerves, remained under dispute. Kolm and Pick found that lack of calcium decreased the irritability of the sympathetic cardiac nerves and increased that of the vagal ones. When the perfusing fluid lacked calcium, adrenalin had quite an atypical, negatively inotropic effect. Instead of producing powerful systolic contractions, it brought on diastolic standstill. This diastolic standstill could promptly be eliminated by paralyzing the vagus with atropine. The value of such an analysis of the calcium effect on the nerves of the isolated heart, however, seemed questionable, since it left out of consideration the effect which calcium undoubtedly has upon the whole vegetative nervous system. More recent investigators, therefore, performed their experiments on whole live animals. Kraus, in 1920, injected a 2.5 per cent calcium chloride solution into live rabbits and guinea pigs. Weak calcium effect, he found, led to respiratory arrhythmia and prolongation of the cardiac cycles—symptoms commonly elicited by stimulation of the vagus. Large doses of calcium, on the other hand, produced a distinct decrease in the irritability of the vagus. Later, Kraus, working in collaboration with Zondek, stated that the effect of calcium corresponded to that of stimulation of the sympathetic nerve. Numerous other workers, however, attributed vagus stimulating qualities to calcium (Billigheimer, Mandelstamm, Brull, Bouckaert and Charnecki). Popescu-Inotesti called calcium an "amphotropic" substance. He observed that

small doses of calcium chloride, given intravenously to human subjects, produced symptoms of stimulation of the sympathetic nerve, such as tachycardia, hypertension, mydriasis, and hyperglycemia, whereas large doses produced symptoms of vagus stimulation, bradycardia, myosis, and hypoglycemia. Up to the present time, however, we still lack an authoritative answer to the question whether calcium stimulates the vagus nerve or the sympathetic nerve.

More recent investigations have revealed one more site of attack of calcium, the coronary arteries. Mancke, in 1930, perfused isolated cats' hearts and found definite increase of the cardiac output when he doubled the calcium content of the perfusing solution. Mancke ascribed that increase of cardiac output to a vasodilator effect of calcium on the coronary arteries. The correctness of this assumption was proved by Hochrein, in 1931, who investigated the blood flow in the coronary arteries of living dogs. He found that intravenous injection of an organic calcium salt, calcium gluconate, definitely dilated the coronary arteries. The effect produced was similar to that of amyl nitrite, glucose, or caffeine, and it could be demonstrated even after the vagus and sympathetic nerves had been severed.

ELECTROCARDIOGRAPHIC STUDIES

Numerous physiological experiments had revealed disturbances of circulatory function produced by calcium. Lowering of the blood pressure was seen by many workers (Rose, Kraus, Brull, Morawitz). Slowing of the heart rate was very frequently observed (Rothberger and Winterberg, Böhm, Sakai, Turan, Kraus, Hirschsohn and Mandl, Brull, Holzlohner, Billigheimer). Disturbances of cardiac rhythm such as respiratory arrhythmia and auriculoventricular block were also seen often. The development of the electrocardiograph finally supplied an accurate method of studying such effects of calcium on living animals and human subjects. Kraus was the first to apply this method. He took electrocardiographic tracings on rabbits and guinea pigs, while a 2.5 per cent calcium chloride solution was being injected into their veins. The first result was that the S-waves became deeper. Then changes in the duration of the cardiac cycle appeared, similar to those seen in man after the application of vagus pressure. When large doses were injected, especially when that was done rapidly, the P-waves disappeared, the S-waves became very deep, and the T-waves became flatter. Kraus was convinced that the flattening of the T-waves was due to calcium and not to the injection of fluid. Injection of large quantities of physiological salt solution, he found, also led to flattening of the T-waves by way of vagus stimulation, and those T-waves could be restored by severing of the vagi. When, on the other hand, the T-waves had become flat after calcium injection, severing of the vagi did not restore them.

The experiments of Kraus were repeated and varied by Fröhlich and Gussenbauer, who also worked on rabbits. After intravenous injection of 2 c.c. of a 10 per cent calcium chloride solution they observed the following: the cardiac cycles showed an average increase from 0.25 sec. to 0.37 sec.; the P-waves remained unchanged; the R-waves became higher; the S-waves became deeper; the QRS interval became wider; the T-waves became flat. Upon injection of larger quantities of calcium chloride, the electrocardiographic changes were more marked: the cardiac cycles varied between 0.3 sec. and 0.45 sec.; the S-waves became very deep; both the P- and T-waves disappeared completely. When the vagus nerve and the sympathetic nerve had previously been paralyzed by atropine, and ergotamine, the calcium injections still led to the same definite electrocardiographic changes.

The experiments of Fröhlich and Gussenbauer as well as those of Kraus analyzed only the initial stages of acute calcium intoxication. In order to observe the full range of calcium effects on the electrocardiogram from small amounts up to lethal doses, Walters and Bowler, in 1924, gave continuous intravenous injections of a 10 per cent calcium chloride solution to dogs. The solution was injected at the rate of 1 c.c. per minute until the animal died. Electrocardiographic tracings were taken during the entire injection. Their results differed considerably from those of the earlier investigators who had worked on rabbits. The first and most striking effect noticed was not slowing, but definite acceleration of rate. Later short, recurring periods of heart-block appeared. With the injection continuing, the QRS complexes became notched, and the T-waves *increased* in amplitude until they finally encroached on the QRS complexes. This was rapidly followed by ventricular tachycardia, ventricular fibrillation, and death. The authors ascribed this death to the occurrence of ventricular fibrillation, and not to calcium rigor or myocardial spasm. Subsequent microscopic examination of sections of the heart muscle showed no evidence of segmentation, fragmentation, or other lesions. The rate at which the injection was given, seemed to be a factor in determining the relative toxicity of any dosage. In two instances, following rapid injection, the calcium content of the heart blood taken immediately after death was twice that of the blood taken from the external jugular vein.

All the electrocardiographic experiments so far mentioned were performed on animals. Up to the present time, no such studies have been made on human subjects, with the exception of a single case, reported by Segall and White. These authors gave their patient an intravenous injection of 75 c.c. of a 2 per cent solution of calcium chloride, at the rate of 5 c.c. per minute. Although marked diuresis resulted, electrocardiograms taken just before and five minutes after the injection showed no difference whatsoever. It is to be noted that no tracing was taken during the course of the injection, which consumed fifteen minutes. Oral administration of

large doses of calcium chloride to eleven patients of the same authors also failed to produce definite electrocardiographic changes.

The discovery of the parathyroid hormone opened up a new approach to the problem. Edwards and Page found a striking similarity between the changes in heart function during hypercalcemia from overdoses of parathyroid extract and those produced by the administration of calcium salts in large amounts. They gave subcutaneous injections of the extract to dogs, at intervals of from two to four hours, and raised the blood calcium to values ranging from 15 to 22 mg. per cent. The heart rate first increased slightly; this was followed by slowing and usually by a marked arrhythmia. Premature beats and a shifting of the pacemaker function frequently appeared. The electrocardiographic records revealed definite but not constant changes. Some tracings showed the P-waves undergoing a progressive increase in height, and direct observation of the heart showed a dilatation of the right auricle. Changes occurred in the amplitude and direction of the T-waves. In the QRS complexes, splintering and widening of the R-wave appeared and became marked as the effects of the extract on the animal progressed.

Electrocardiographic manifestations which Gold and Edwards observed on dogs after injection of calcium chloride and after administration of parathyroid extract varied considerably in different animals. The first dose generally brought on sinus irregularity. Later, there were disturbances in the pacemaker, the P-waves sometimes being upright, inverted, high and low in the same lead. The T-waves showed similar variations. There were also varying degrees of impairment of conduction, with S-A block, A-V block, and dropped ventricular beats. Large doses of either agent usually produced ventricular tachycardia.

Finally, another series of observations was made which referred not to the *form*, but to the *duration* of the ventricular complexes. Carter and Andrus, in 1922, found that in experimental lack of calcium the Q-T interval of the electrocardiogram was lengthened. To correlate these observations with conditions that obtain in human subjects, Carter and Andrus made electrocardiographic studies on clinical conditions associated with changes in the serum calcium level. They collected six cases of infantile tetany and three cases of adult tetany. For calculating the normal duration of systole, they employed the formula of Bazett. In all six cases of infantile tetany, the Q-T interval was constantly prolonged. The prolongation decreased as the serum calcium level rose under treatment. Similarly, the Q-T interval occupied a smaller percentage of the cardiac cycle as the calcium concentration in the serum increased. In each of the three cases of adult tetany, the Q-T interval was prolonged more than 30 per cent above Bazett's formula. The important findings of Carter and Andrus were later confirmed by White and Mudd. These authors saw prolongation of the Q-T interval beyond the normal in two cases of tetany, with a return to normal as the serum calcium level rose.

In concluding this series of electrocardiographic observations, one more report may be mentioned briefly. Wolffe and Bellett, in three cases, were able to terminate attacks of paroxysmal tachycardia by slow intravenous injection of 20 c.c. of calcium gluconate or afenil.

PHARMACOLOGICAL EXPERIMENTS

Reviewing the various effects of calcium on the heart in physiological and electrocardiographic experiments, one is impressed by their similarity to the effects of the best known cardiotonic drug—digitalis. This similarity was noted by pharmacologists at an early period and became the subject of intensive investigation. In 1910, Werschinin, working on frogs' hearts, found that an increase of calcium salts in the Ringer's fluid enhanced the systolic effect of strophantine. Clark, in 1912, went so far as to conclude that the systolic action of digitoxin was actually dependent upon the presence of calcium.

The first comprehensive investigation of this problem was made by Loewi, in 1917. He found that strophantine failed to produce the characteristic systolic standstill of the isolated frog's heart when a calcium-free Ringer's fluid was used. As soon as calcium was added, however, tetanic contraction appeared. The systolic effect of strophantine, Loewi concluded, depended solely upon calcium. Loewi asserted that strophantine merely sensitized the heart for calcium, and that strophantine effect was in reality calcium effect. Loewi supported this theory by further experiments in which he attempted to demonstrate that the characteristic digitalis effects, increase of systole, slowing of the rate, irregularity, systolic or diastolic standstill, could all be accomplished by calcium alone.

S. G. Zondek also attempted to prove Loewi's theory. Frogs' hearts brought to standstill by quinine or arsenic started beating again when Zondek increased the calcium content of the Ringer's fluid. When he added strophantine instead of calcium, the hearts previously arrested by quinine or arsenic also started beating again. Calcium, therefore, could here be replaced by strophantine. On the other hand, Zondek was able to prevent the strophantine effect by the addition of any one of the antagonists of calcium, by potassium as well as by quinine or arsenic. He concluded that certain poisons, e. g., quinine and arsenic, affected the heart muscle in the same manner as potassium ions; others, e. g., digitalis, in the same manner as calcium ions. One important difference, however, was noted by him: Potassium and calcium effects set in promptly and passed rapidly, whereas the effects of quinine, arsenic, and strophantine were slow in appearing, but lasted.

The work of Loewi and Zondek started a controversy which lasted for several years. Loewi's whole theory was based upon the one finding, that strophantine had no effect on the heart in the absence of calcium, and this finding was not confirmed by a number of subsequent investigators, such

as Hoffmann and Schlossmann. In 1926, Mandelstamm undertook to check Loewi's findings in experiments done on the heart of a warm-blooded animal, the rabbit. Mandelstamm admitted the fundamental importance of calcium for the contractility of the heart muscle, and he also confirmed the early finding of Werschinin that increase of calcium in the perfusing fluid enhanced the effect of strophantine. But his results did not agree with those of Loewi at all. Strophantine did not sensitize the heart for calcium, and its action was entirely independent of the presence of calcium. Hearts which were perfused with a calcium-free Ringer's fluid and thereby deprived of their calcium, still responded to strophantine. In the following year, Fischer, working on frogs' hearts, found that the course of digitoxin poisoning was in every respect the same, whether calcium was present or absent. This course was not altered when it was either preceded or accompanied by the administration of calcium. If, on the other hand, digitoxin effect preceded the administration of calcium, even if by only a few minutes, then comparatively small doses of calcium produced tonic contraction of the heart. Fischer concluded that digitoxin sensitized the heart for calcium. But he considered that sensitization as wholly nonspecific. Digitoxin, he said, increased the general irritability of the heart, with the result that tonic contraction would be produced by any stimulus, not only by calcium but also by potassium or ethyl alcohol, agents which fail to produce such contraction on the *normal* heart. This last conclusion was also reached by another investigator, Cloetta. Cloetta's experiments demonstrated clearly that calcium and digitalis have different points of attack and that their actions cannot be identical. Finally, this problem was investigated by Nyiri and DuBois, who showed that neither lack of calcium nor atropine paralysis of the vagus nor adrenalin stimulation of the sympathetic nerve changed the course of digitalis poisoning, and they stated that calcium and digitalis were not essentially related in their action, in spite of the similar features of their effect.

While the theories of Loewi and Zondek were thus disproved, the synergism of calcium and digitalis remained an established fact. Even a quantitative analysis of this synergism became possible. Gold and Edwards accomplished such an analysis by producing hypercalcemia in dogs and then injecting ouabain intravenously. The hypercalcemia was brought about by the injection of calcium chloride or of parathyroid hormone, which raised the serum calcium level to 20 and 25.6 mg. per cent respectively. Frequent electrocardiograms were taken on all their animals. There was strong evidence of the synergism between calcium and ouabain, and this persisted even after electrocardiographic effects of calcium action had disappeared. The injection of calcium chloride reduced by approximately 40 per cent the fatal dose of ouabain as well as the dose necessary to induce idioventricular beats. For animals with hypercalcemia produced by the parathyroid hormone, the fatal dose of ouabain either was the same as for normal animals or was greatly diminished.

CLINICAL OBSERVATIONS

The use of calcium for the treatment of heart disease was advocated as early as 1841 by Blake. In 1907, Sir Lauder Brunton recommended it and suggested that the great benefit one frequently observes from milk diet might be due, in part, at least, to the large quantities of calcium salts which the milk contains. The treatment never became popular until Singer, in 1921, first introduced intravenous injections of calcium chloride for the treatment of heart failure with edema. Following the injections, Singer observed slight slowing of the pulse, decrease in blood pressure, and, what he especially emphasized, markedly increased diuresis. Stimulated by the pharmacological experiments of Loewi, Singer then combined small doses of calcium, 1 c.c. of a 10 per cent calcium chloride solution, with digitalis, and reported a better diuretic effect than could be obtained with digitalis alone. He even believed that calcium prevented some of the gastric disturbances set up by digitalis. That the calcium effect lasted a much shorter time than that of digitalis, he admitted, and he was aware of the fact that no calcium was stored in the heart.

Singer's publication is open to much criticism, especially if viewed in the light of our more recent knowledge on digitalis. Calcium will surely not prevent any gastric disturbances caused by digitalis. Such disturbances depend to a great extent on the quantity of digitalis given, and only if that quantity is diminished because of simultaneous calcium administration, are gastric disturbances less likely to occur. Furthermore, Singer never differentiated between diuretic and cardiotonic effects. He did not consider the possibility that calcium might affect the edema itself without acting on the heart in any way. Singer's reports, nevertheless, served to popularize the treatment for a while. They were soon followed by a number of papers by other clinicians advocating the use of calcium as an adjuvant to digitalis. (Cheinisse, Loewenberg, Hellmann and Kollmann.) Nathorff, in 1924, reported experiences with simultaneous *oral* administration of 0.025 gm. powdered digitalis and 0.2 gm. calcium lactate, combined in one tablet. He stated that he compared the effect of digitalis alone with that of the digitalis calcium combination, and while he found no difference in some cases, in many others he was convinced that the effect of the combination was more rapid. It is to be noted how small the amounts of calcium were which Nathorff used. It is now evident that such minute doses did not raise the blood calcium level, and it is, therefore, hard to understand how they could have exerted such marked effects on the heart.

More definite were the reports of a cardiotonic effect of *intravenous* calcium chloride injections which Petzetakis published in 1924. He found that doses of 0.1 to 1.0 gm. in 10 per cent solution, raised the blood pressure, increased the force of the cardiac contraction, slowed the pulse, and increased the irritability of the vagus nerve. He saw that calcium eliminated extrasystoles, and stopped attacks of paroxysmal tachycardia. In

one case of auricular fibrillation, it restored regular sinus rhythm, after digitalin and ouabain had failed to do so.

Another author who repeatedly advocated the combined calcium digitalis therapy was Billigheimer. He observed that intravenous injection of a 10 per cent calcium chloride injection led to slowing of the heart rate, which reached its lowest point within two or three minutes, and which lasted twenty-five to thirty minutes. But when the calcium injection was given to a digitalized patient, the slowing of the heart rate lasted four to five hours instead of twenty-five minutes. Billigheimer considered his observation as proof of the statement that digitalis sensitized the human heart for calcium. Furthermore, he emphasized the fact that calcium administration had the same effect on the heart rate as stimulation of the vagus. When he produced tachycardia by an injection of adrenalin and thereafter injected calcium, the rate dropped at once from 120 to 70 or even 60 beats per minute. When, on the other hand, tachycardia was produced by injecting atropine, which paralyzes the vagus, the subsequent calcium injection had no effect whatever on the heart rate.

If the cardiac action of calcium is in any way comparable to that of digitalis, then it would be expected to have a similar effect on auricular fibrillation. Segall and White gave calcium chloride by mouth in large doses to patients with auricular fibrillation, but noted no digitalis-like action whatsoever. Neither in these cases nor in those with regular rhythm was there any evidence to indicate that calcium chloride had any effect at all on the circulatory mechanism.

Yet, in spite of such discouraging clinical reports as the one last mentioned, there still exists a possibility that calcium may ultimately prove of some value in the treatment of heart disease. Weighty endorsement was recently given to it by Cloetta. He stated that calcium and digitalis have different points of attack but may, nevertheless, be combined to obtain a summation of effect. He advocated intravenous injections of 10 c.c. of a 10 per cent calcium chloride solution as sufficient to raise the calcium level to double the normal amount. With this method of calcium administration, a decided intensification of digitalis action was obtained. But thirty minutes after the injection, the blood calcium became normal again so that the summation effect of the two substances disappeared. Cloetta advised, therefore, that calcium be given by mouth as well. That it is possible to raise the blood calcium level by oral doses of calcium was proved by Kahn and Roe, who found that five gram doses of calcium lactate gave an average maximum elevation of 80 per cent between the sixth and seventh hour, and maintained an elevation above normal for nine hours.

With the introduction of a new, organic calcium salt, calcium gluconate, an even better means of administering calcium orally was found, since that salt produces much less gastric irritation and yet is equally able to produce elevation of the blood calcium level (Rothlin, Lieberman).

SUMMARY

Physiological experiments establish the importance of calcium for maintaining the contractility of the heart and demonstrate five different sites of attack of calcium: (a) the contractile elements, (b) the idioventricular centers, (c) the conductive system, (d) the nerves of the heart, (e) the coronary arteries.

Electrocardiographic studies show that calcium produces definite but variable changes in the form of all waves, various disturbances of rhythm, and a shortening of the electrical systole.

Pharmacological experiments prove a synergism of calcium and digitalis in animals.

Clinical observations show the diuretic effect of calcium, but fail to prove a direct cardiac effect.

In reviewing all these investigations into the effect of calcium on the heart, we find two facts of outstanding significance. Animal experiments, both physiological and pharmacological, prove conclusively enough that calcium has definite effects on the heart. Observations on human subjects, both clinical and electrocardiographic, however, fail as yet to show convincingly that calcium has any usefulness in cardiac therapy. Nevertheless, it is possible that future clinical investigations may demonstrate such usefulness. The mild diuretic effect of calcium, which is not discussed here, is proved, but that effect is produced by influencing the water metabolism in the tissues. As to its direct cardiac effect, so much is certain that any future study of it will have to be more than a collection of clinical impressions. The experiments on animals, in particular those by Boehm and those by Walters and Bowler, show clearly that, in order to be effective, the doses of calcium have to be so large as to raise the blood calcium level by more than 100 per cent. Future clinical studies, therefore, will have to include blood calcium determinations and possibly quantitative analyses of calcium metabolism. Any results which are not accompanied by a rise in blood calcium must be subjected to careful scrutiny.

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Selected Abstracts

Hyman, Albert S.: Resuscitation of the Stopped Heart in Intracardial Therapy. II. Experimental Use of an Artificial Pacemaker. Arch. Int. Med. **50:** 283, 1932.

Stimulation of the stopped heart by electrical methods has previously failed because most investigators have attempted to reactivate the heart by neurogenic excitation.

When electric current has been applied directly to the heart, it has been done by placing the entire organ in the electric circuit; the result has been that the heart is unable to maintain its normal cycle. When strong currents have been used, the factors discovered in electrocution are seen to be present.

In using a clinical needle through which is carried an electric impulse, and in having the two electrodes so close together that only a small pathway is concerned in the electric arc established by the heart muscle, an irritable point is produced.

This irritable point becomes the focus from which an excitation wave may spread over the heart muscle, the excitation wave developing and spreading according to normal physiological conditions. The impulse released from the pacemaker needle differs in no way from that produced by the prick of an injecting needle except that in the latter instance only one stimulus is developed, while in the former any number can be delivered to the heart muscle.

An apparatus has been constructed which attempts to simulate the excitation wave developed by the normal sinus nodal pacemaker; it consists of a special current generated by a magneto which is activated by a spring motor, making it instantaneously available at any time, at any place and under all circumstances, as it is an independent electric unit. The current from this generator can be so regulated that the impulses are delivered to the needle point at a constant regular rate varying from 30 to 120 beats per minute.

The needles are carried in hermetically sealed tubes that have been sterilized; in the puncture procedure the same aseptic precautions must be observed as in any other sterile injecting manipulation. The needle is inserted into an insulated handle which carries the terminals of the electric circuit from the generator. A convenient switch on the handle permits the current to be introduced into the needle at will.

Experimental animal studies have shown that the arrested heart is rapidly returned to automatic sinus activity after the response to the artificial pacemaker has restored some of the normal circulatory balance. Typical graphs are presented which show the electrocardiographic exposition of the events that take place in the heart when the artificial pacemaker is applied to the stopped heart.

The use of the artificial pacemaker in the normally beating heart is also shown, and the relative harmlessness of the procedure is indicated, the result being the development of a regular extrasystolic arrhythmia. The artificial pacemaker impulse is followed by an ectopic beat from that area of the heart stimulated.

The question of utilizing the artificial pacemaker in certain gross irregularities of the heart is also discussed, but this field still requires considerable investigation before conclusions of any type can be considered.

In view of the possible advantageous results to be anticipated by the use of the artificial pacemaker in the arrested heart which does not respond to the usual methods of therapy, the employment of this method is suggested. When patients have succumbed to disease processes, an attempt can be made to renew automatic cardiac activity by the use of the artificial pacemaker without in any way jeopardizing their condition.

When correctly used, the artificial pacemaker may prove to be of inestimable value in the restoration of those patients now succumbing to cardiac arrest; employed together with other established life-saving procedures it may well be included in every physician's armamentarium against the final struggle with death.

Hooker, D. R., Kouwenhoven, W. B., and Langworthy, O. R.: The Effect of Alternating Electrical Current on the Heart. Am. J. Phys. **103:** 444, 1933.

Working with the dog heart in fully anesthetized animals, the authors have studied the effects produced by different values of 60 cycle alternating current. This was used because of the ease with which permanent ventricular fibrillation may be established by electrical stimulation and because the main interest was to investigate the value of electric countershock in overcoming ventricular fibrillation. Alternating currents of five or more amperes when passed through the body for one-half to five seconds will not produce ventricular fibrillation. However, the usual house circuit of 110 volts similarly applied will invariably produce fibrillation because the current that flows presumably is not sufficient to inhibit the heart. One milliampere of current applied directly to the ventricular musculature is sufficient to cause fibrillation, and the extreme ventricular apex is as sensitive as any other point on the ventricles.

With the electrodes applied directly to the heart, currents of 0.4 ampere for five seconds will cause fibrillation and currents of 0.8 ampere or more will stop fibrillation. A current of 0.8 ampere will not induce fibrillation, and a current of 0.45 ampere will not stop fibrillation. In the intact animal with the electrodes on either side of the thorax, the current spreads out over the body tissues. In order to obtain a sufficient current through the heart to arrest fibrillation, the countershock current must be increased to a value of at least four or five amperes.

Following the countershock, the ventricles are quiescent for a brief period. When contractions began they were very feeble but quickly increased in vigor, and the circulation was re-established if fibrillation has not continued for long. If fibrillation has lasted for two minutes or more, spontaneous recovery of effective beats will not follow. Under these circumstances, cardiac massage may be of signal benefit.

Of even greater assistance than cardiac massage is the central carotid injection of adrenalin in a salt solution. Best results were obtained by injecting under a pressure of 150 mm. of mercury from 5 c.c. to 10 c.c. per pound of a solution made up of calcium chloride 0.046 per cent in sodium chloride 0.9 per cent containing heparin, saturated with oxygen and warmed to body temperature. To this mixture 2 c.c. adrenalin chloride 1:1000 should be added.

Stewart, Harold J., and Cohn, Alfred E.: Studies on the Effect of the Action of Digitalis on the Output of Blood From the Heart. II. The Effect on the Output of the Hearts of Dogs Subject to Artificial Auricular Fibrillation. J. Clin. Investigation **11:** 897, 1932.

During auricular fibrillation when the ventricular rate is rapid, the cardiac output per minute is less than it is during the normal slower sinus rhythm. In consequence of this abnormal rhythm in intact unanesthetized trained dogs, the heart increases in size. This conclusion is based on a larger number of observations than was possible in an earlier paper. When the cardiac output is diminished and the heart is dilated due to artificial auricular fibrillation, the administration of digitalis results in increase in cardiac output and decrease in cardiac size. When the normal rhythm returns, the heart being of course still under the influence of digitalis, either the output increases, the size remaining unchanged (from that in the fibrillatory state), or both output and size decrease.

The observations show, as do the ones next to be reported, that digitalis has the same action in normal and in pathological hearts; it decreases cardiac size (an effect on tone). The amount of cardiac output which results from this action depends upon the initial size of the heart; it decreases in normal hearts and increases in dilated ones. In a dog, the subject of edema due to taking sodium bromide, the administration of digitalis increased cardiac output, decreased cardiac size and increased the extent of ventricular excursions.

Stewart, Harold J., and Cohn, Alfred E.: Studies on the Effect of the Action of Digitalis on the Output of Blood From the Heart. III. Part 1. The Effect on the Output in Normal Human Hearts. J. Clin. Investigation **11**: 917, 1932.

The effect of giving digitalis to six normal individuals was studied with particular reference to its effect on cardiac output, on cardiac size and on venous pressure. The following phenomena were observed: (1) the output of blood from the heart decreased; (2) the size of the heart diminished; (3) slight decrease in cardiac rate occurred; (4) the effects were at a maximum four to twenty-four hours after giving the drug; (5) significant changes did not occur in the levels of arterial and venous pressure; (6) changes in form, sometimes slight, of the T-waves of the electrocardiogram occurred in each instance and were present as early as two and one-half hours after the drug was given; (7) as an effect of digitalis wore off (forty-eight hours to three weeks), output, size, rate and the T-waves of the electrocardiogram returned toward their initial values; (8) a correlation was not established from these data between decrease in cardiac output and change in the level of venous pressure.

Stewart, Harold J., and Cohn, Alfred E.: Studies on the Effect of the Action of Digitalis on the Output of Blood From the Heart. III. Part 2. The Effect on the Output of Hearts in Heart Failure With Congestion, in Human Beings. J. Clin. Investigation **11**: 933, 1932.

A consequence of the action of digitalis is to decrease the volume output of blood per minute from the heart in normal human beings and to decrease its size. The volume output of blood per minute from the heart which is in failure is diminished and its size is larger than when it is in a state of compensation.

Following the administration of theocalcin in patients during heart failure, cardiac output increases and cardiac size and venous pressure diminish. Giving digitalis increases the volume output of blood per minute from failing hearts and decreases the size.

Digitalis, it is thought, has similar, perhaps identical, actions both in normal and in diseased hearts; it decreases cardiac size and increases the extent of ventricular contraction. The consequence of these actions is that the volume of the cardiac output which results differs, depending on an initial difference in size of the ventricular cavities in the two situations. In the one, the normal heart, it becomes too small; in the other, the diseased heart, it develops a suitable size.

Chapman, C. W., and Morrell, C. A.: On the Biological Assay of Digitalis and Strophanthus. J. Pharmacol. & Exper. Therap. **46**: 229, 1932.

A frog method for the biological assay of digitalis and strophanthus preparations is described in detail. The method eliminates the effect of individual variation in the frogs and variations which occur from time to time. The results of a series of assays on tinctures of digitalis and strophanthus are presented.

The official U. S. P. X. method is discussed with the method described. The wide fluctuations in the M. S. D. values for ouabain are attributed to neglect of the effect of individual differences in the sensitivity of the frogs. Seasonal, diurnal and species variations are discussed.

It is maintained that the frog method, using the technic described, combines accuracy, simplicity and economy to a greater degree than do other methods.

Anthony, Albert J., Cohn, Alfred E., and Steele, J. Murray: Studies on Cheyne-Stokes Respiration. J. Clin. Investigation 11: 1321, 1932.

The influence on Cheyne-Stokes respiration of breathing varied mixtures of carbon dioxide and air has been studied in periods both of short and of long duration. Increase in concentration of carbon dioxide in the air inhaled prolongs the respiratory phase and decreases the apneic phase until continuous breathing appears. Increase in the concentration of oxygen up to 80 per cent in the air inhaled prolongs the respiratory phase markedly. The duration of apnea is sometimes increased and sometimes remains constant. Inhaling oxygen in greater concentrations than that of air does not usually result in continuous breathing.

If the treatment of Cheyne-Stokes respiration has as its object the restoration to normal of the concentrations of the gases in the blood, then bringing about continuous respiration need not of itself be regarded as improvement, because continuous breathing alone does not necessarily mean that the ventilation is more nearly sufficient. For example, two patients with Cheyne-Stokes respiration were observed in whom the last stage of their disease was accompanied by an increase in cyanosis and return to continuous breathing at one and the same time. If the object of treatment is to bring about continuous respiration, then inhalation of carbon dioxide in a chamber may be attempted using the smallest concentration necessary to assure this result. To decrease the rhythmic recurrence of lack of oxygen, the effect of inhalation of oxygen in the chamber may also be utilized as is shown by the analysis of blood of patients while they are in the oxygen chamber.

Palmer, Robert Sterling: The Hypotensive Action of Potassium Sulphocyanate in Hypertension. Am. J. M. Sc. 8: 473, 1932.

Thirty-five well controlled patients, most of them showing the effects of continued arterial hypertension have been treated by potassium sulphocyanate. This drug when used in sufficient dosage caused a definite and marked lowering of the arterial blood pressure in 31 per cent of the patients.

Toxic effects were skin rashes, gastrointestinal symptoms and central nervous system symptoms such as acute apprehension and excitement which may be severe enough to constitute a toxic psychosis. Weakness may accompany the use of the drug but is probably not a toxic effect and does not necessarily contraindicate its use. Angina pectoris in those subject to this symptom may be increased and in some patients may be induced by use of this drug. Toxic effects were reduced to the minimal by carefully controlled dosage.

Limited observation of the use of the drug in combination with a general régime including rest and diet suggests that it may be of value, though these results may not be referred to in accurately appraising the hypotensive action. Generally speaking it may be said that the hypotensive effect is not lasting and that a second or third such effect after the drug is once discontinued is more difficult to obtain.

Prodger, Samuel H., and Ayman, David: Harmful Effects of Nitroglycerin. Am. J. M. Sc. 184: 480, 1932.

Nitroglycerin in therapeutic doses was administered to 110 patients under direct observation. Alarming toxic reactions were observed in four cases. In two instances the blood pressure became indeterminable and the pulse could not be palpated. Heart-block developed in one of these, and in the other the course of a cardiac infarction was thought to be unfavorably influenced. A record was made of the electrocardiographic changes

which occurred during the reactions in these two cases. In the other two cases there were, as evidence of toxicity, marked slowing of the pulse rate, great drop in blood pressure and severe constitutional symptoms.

Careful supervision of the patient is advised when the first dose of nitroglycerin is administered in order that those who have an idiosyncrasy to it may be discovered and possible dangerous reactions avoided. A small initial dose is advised. The possible harmful effects of nitroglycerin in coronary thrombosis are discussed.

Gold, Harry, and Modell, Walter: The Action of Quinidine on the Heart in the Normal Unanesthetized Dog. J. Pharmacol. & Exper. Therap. **46**: 357, 1932.

The effect of intravenous injections of quinidine in therapeutic and toxic doses on the heart of normal unanesthetized dogs was studied electrocardiographically.

In both therapeutic and convulsive doses, quinidine does not produce slowing but acceleration of the sinus rate. Acceleration occurs in vagotomized dogs as well, especially in those cases in which the vagotomy does not result in an extremely rapid heart rate. In doses up to those causing convulsions, quinidine does not produce any prolongation of A-V conduction. Frequently the P-R interval is shortened simultaneously with the sinus acceleration. The drug causes prolongation of intraventricular conduction. This is sometimes in evidence with therapeutic doses but is most constant and pronounced after larger doses.

A negative T-wave becomes positive and a positive T-wave increases in amplitude. This effect of quinidine is constant in normal dogs and is a very sensitive reaction, occurring after doses as small as 2 mg. and may appear without any other changes in the electrocardiogram.

All the effects noted in the study are fleeting, coming on frequently within less than a minute after the injection and disappearing, in many cases, in less than fifteen minutes. These results are in some respects at variance with those reported in the literature. It is suggested that anesthesia and various operative procedures used in most of the previous studies on animals may be chiefly responsible for the differences.

Stieglitz, Edward J.: Therapeutic Results With Bismuth Subnitrate in Hypertensive Arterial Disease. J. Pharmacol. & Exper. Therap. **46**: 343, 1932.

The present report deals with a series of 30 cases of hypertensive disease treated with bismuth subnitrate and observed over a period of several years. The basis of selection of these patients was the duration of carefully controlled observation and that no active initiating etiological factors were treated during or shortly preceding the period of observation. The therapeutic results obtained are most encouraging and gratifying.

It is believed that not only does bismuth subnitrate reduce the arterial tension in spastic hypertonia during the period over which it is administered, but, if the administration be prolonged sufficiently to permit of arteriolar rest, the arteriolar hypertonia frequently does not recur. It assists in reduction of the physiological burden of the injured structures, namely the medial musculature of the arterioles.

In the presence of extensive arteriolarsclerosis or active etiological sources of arteriolar irritation, bismuth subnitrate is inadequate, as would be any other mild vasodilator. In angina pectoris associated with hypertensive disease, bismuth subnitrate appears to reduce the frequency and severity of anginal attacks.

Porter, Elsie: The Therapeutic Use of Drugs of the Digitalis Group. Quarterly J. M. **2**: 33, 1933.

A massive calculated dose of the tincture of digitalis at the rate of 0.125 c.c. per lb. of body weight of the patient, when administered by mouth in a single draught, is

the method of choice in treating cases of auricular fibrillation, because a perfectly good result can be obtained with certainty in six to eight hours.

In cases of vomiting from congestive failure an equally good result may be obtained by giving a similar massive dose per rectum, calculated at the rate of 0.1 c.c. per lb. of body weight.

In very urgent cases, where a still more rapid action is required, a similar result may be obtained within thirty minutes by the administration of a single intravenous dose of 1/33 gr. of strophanthin. The site of action in all three routes is similar, i. e., that they all act via the vagus, as shown by "vagal release" with atropin.

Cases of auricular fibrillation should be given the advantage of being treated by one or other of the methods described, in order that their discomfort may be relieved in a day, instead of having it prolonged to a week by the use of older methods.

Hansen, Olga S., and Maly, Henry W.: The Effects of Thoracoplasty on the Heart. Am. Rev. Tuber. **27**: 200, 1933.

In an attempt to determine the effects of thoracoplasty on the heart as evidenced by the electrocardiogram, 57 cases have been studied by means of electrocardiograms and x-ray films, before and after the collapse. Thirty cases of uncomplicated pulmonary tuberculosis have been taken for controls. It has been shown that the intrathoracic pathological involvement incident to thoracoplasty almost invariably displaces the heart more or less to one side or the other but most frequently toward the unaffected side. The electrocardiograms also show a high incidence of postoperative change, but these changes are neither consistent nor predictable, being in agreement with the x-ray findings in only a third of the cases. It would seem impossible to predict the probable electrocardiographic change from a study of the x-ray pictures or, conversely, to guess the type of x-ray findings from looking at the electrocardiograms. It is probable that the electrical axis may be influenced by rotation of the heart on its longitudinal axis by fibrotic tissue affecting at times the base, and at times the apex anteriorly or posteriorly. It is probable that other factors such as bed rest, toxemia and weight changes may affect the form of the electrocardiogram, since the control patients who had no gross mechanical changes were also variable in their complexes.

There has been no evidence of disturbance in conduction or of myocardial damage in the electrocardiograms. Autopsy has shown no abnormality in heart weight nor more evidence of myocardial degeneration than is found in other patients dying of tuberculosis. Some of the changes in QRS amplitude probably represent changes in muscle tone associated with reduction of toxemia and increase in exercise and would appear regardless of the mechanics of collapse. The changes found in the electrocardiogram are probably due to extrinsic factors and bear no relationship to the condition of the heart muscle.

Camp, Paul D., and White, Paul D.: Pericardial Effusion: A Clinical Study. Am. J. M. Sc. **184**: 782, 1932.

The authors have studied the clinical and pathological data on 126 cases containing over 100 c.c. of pericardial fluid found at postmortem examination over a period of ten years occurring among 95,542 cases admitted to the hospital and among 1,729 necropsies. They conclude that without the presence of an acute fibrous pericarditis, the diagnosis of pericardial fluid is likely to be missed unless the effusion amounts to over 500 c.c. Of the 126 cases, a correct clinical diagnosis of pericardial effusion was made only 6 times.

To establish a clinical diagnosis of pericardial effusion, all signs and symptoms must be carefully looked for and analyzed and roentgen ray studies employed in all cases except a very few, where the effusion is so large and rapid in its development that the clinical diagnosis is easily made at once.

Gouley, B. A., Bellet, Samuel, and McMillan, Thomas M.: Tuberculosis of the Myocardium. Arch. Int. Med. **51**: 244, 1933.

Six cases of tuberculosis of the myocardium are reported. Four of the patients were males and two were females. Four were negroes and two were white people. The ages of the patients were 16, 16, 26, 46, 51 and 17 years. These cases represent the different types of tuberculous myocarditis that have hitherto been reported. A simple classification is suggested, based on the mode of dissemination and the type of lesion; (a) myocardial tuberculosis, secondary to mediastinal glandular and pericardial tuberculosis and (b) as part of systemic miliary tuberculosis.

Involvement of the coronary arteries in one case in an unusual degree and in other cases to slight degree is reported, and the various types of tuberculous arteritis are described: (a) diffuse tuberculous arteritis, involving all the vessel coats; (b) intimal tubercle without involvement of other vessel coats as a result of blood borne infection; and (c) a type of arterial involvement by tuberculosis (contact arteritis) previously not described in the heart, affecting not only the small but also the large coronary arteries and leading to narrowing of their lumens and even to complete occlusion.

The occasional similarity of rheumatic and tuberculous myocarditis is noted, and a differential diagnosis is outlined. The probability of ectopic rhythm resulting from the tuberculous infiltration of the right auricle is discussed.

Horton, Bayard T., and Brown, George E.: Thromboangiitis Obliterans Among Women. Arch. Int. Med. **50**: 884, 1932.

Although approximately 700 cases of thromboangiitis obliterans have been observed among men at the Mayo Clinic, the present report of 10 cases is the first series among women to be put on record. The diagnosis in three of these cases was proved by a study of the pathological changes in the occluded arteries and veins. The authors are of the opinion that this disease has a higher incidence among women than is brought out by this study. The failure to recognize the disease is due probably to the facts that it is relatively mild among women and that the diagnosis is overlooked. Three of the patients in the series were of Jewish extraction; their disease was more severe than in the 7 gentiles. A similar clinical impression was gained in the series of men; the disease of the Jewish patients seemed more serious and intense than that in the other races.

Four patients were treated by bilateral lumbar sympathetic ganglionectomy; one of these also had bilateral cervicothoracic sympathetic ganglionectomy. One patient had an amputation of the right leg and the other patients were treated medically. The treatment, for the most part, has proved satisfactory. The disease among women apparently runs a similar but definitely milder course than among men.

Stehle, R. L.: A Method for Studying Variations in Coronary Inflow During a Series of Cardiac Cycles, or for Determining Inflow Rates Generally. J. Pharmacol. & Exper. Therap. **46**: 471, 1932.

The method is described for use as outlined in the succeeding paper. It is a modification of the Langendorff method.

Stehle, R. L., and Melville, K. I.: The Influence of the Heart Beat Upon the Flow of Blood Into the Coronary Arteries. J. Pharmacol. & Exper. Therap. **46**: 477, 1932.

The method of studying coronary inflow described in the preceding paper has been applied to the rabbit's heart. The results show that the inflow begins late in diastole and continues into systole. It is not restricted to diastole or to systole. In contradistinction to observations by Hochrein, these experiments indicate that the maximum flow is not restricted to an instant but lasts through a definite period. The authors

believe that their results are in agreement to a considerable extent, with those obtained by Anrep. The authors also compare their results with the data published by Roessler and Pascual.

Katz, Louis N., Hamburger, Walter W., and Rubinfeld, Samuel H.: Observations on the Effects of Oxygen Therapy. II. Changes in the Circulation and Respiration. Am. J. M. Sc. **184**: 810, 1932.

A comparison of the effects of oxygen therapy on the circulation and respiration of a group of cardiac and noncardiac patients was used as a check on the clinical impressions and to determine whether these changes preceded, accompanied or followed the clinical improvement. A modified direct venous pressure method is described and also a simple clinical method of determining minute volume of respiration.

Oxygen therapy tended to decrease the vital capacity slightly; it caused no significant changes in arterial and venous pressure. An increase in the amplitude of QRS and an increase in the size and duration of the T-wave were found in the majority of cases during exposure to an oxygen-rich atmosphere.

Oxygen therapy was found to result in (1) a slowing of the heart by causing a sinus bradycardia, (2) a decrease in minute volume of respiration, and (3) an increase in the length of time the breath could be held. These changes tend to occur as readily in the noncardiac case as in the cardiac and in the latter in spite of advancing failure. These changes are primarily the result of the oxygen-rich environment and seemed in part, at least, independent of relief of arterial anoxemia. These changes in heart rate, in breath holding ability and in minute volume of respiration are in themselves beneficial and may be ways, aside from relief of arterial anoxemia, by which oxygen therapy may act beneficially in cases of heart failure. No slowing of ventricular rate occurred in cases with auricular fibrillation, and less beneficial effects may be expected from oxygen therapy in such cases. No direct diuretic effect was observed as a result of oxygen, either in the edematous or nonedematous patients.

Cohn, David J., Katz, Louis N., Soskin, Samuel, and Hamburger, Walter W.: Observations on the Effects of Oxygen Therapy. III. Blood Chemical Changes. Am. J. M. Sc. **184**: 818, 1932.

The function of oxygen therapy is not to attack the underlying causes of the disease but to give the patient the benefit of as high a blood oxygen saturation as possible. It is conceivable that some of the benefits of oxygen therapy may be produced in other ways besides the improvement of arterial anoxemia. However, the major benefit of oxygen therapy is the increase in oxygen saturation of the arterial blood, thus relieving the arterial anoxemia and its effects.

Asher, A. Graham: Graphic Registration of Heart Sounds by the Argon Glow Tube. Arch. Int. Med. **50**: 913, 1932.

A new method for photographing heart sounds has been described, the Argon Glow tube being used. Once the necessary apparatus was set up, the method was found to be simple. It could detect the ordinary and obscure heart sounds. Illustrations of some of its uses in clinical cases are described, and suggestions for its further applications are offered.

Hudson, Charles L., Moritz, Alan R., and Wearn, Joseph T.: The Extracardiac Anastomoses of the Coronary Arteries. J. Exper. Med. **56**: 919, 1932.

In a series of experiments planned for the purpose of injecting the vessels in the heart valves, a colloidal suspension of carbon particles was injected into the coronary arteries of human hearts which had been excised at autopsy. When one came to

study the injected specimens, it was soon observed not only that the vessels in the heart were filled with the carbon particles but also that the arteries in attached flaps of the parietal pericardium contained the injection mass. Further observation showed that an extensive network of vessels in the adventitia of the aorta and pulmonary artery was also injected. These observations led to a more thorough study of the extracardiac anastomoses of the coronary arteries.

It was found that widespread anastomoses of the auricular branches and the coronary branches to the pericardial fat with the pericardiacophrenic branches of the internal mammary arteries and the anterior mediastinal, pericardial, bronchial, superior and inferior phrenic, intercostal and esophageal branches of the aorta were present. The most extensive anastomoses between the cardiac and extracardiac vessels were around the ostia of the pulmonary veins. It was possible not only to demonstrate the passage of injection mass from the coronary arteries into the vessels of surrounding structures, but also to show vessels in the heart injected through the thoracic branches of the aorta.

This rich potential extracardiac coronary collateral circulation is probably of significance in compensating for sclerosis of the large trunks of the coronary arteries.

Moritz, Alan R., Hudson, Charles L., and Orgain, Edward S.: Augmentation of the Extracardiac Anastomoses of the Coronary Arteries Through Pericardial Adhesions. J. Exper. Med. **56:** 927, 1932.

The examination of four hearts with partial or complete obliteration of the pericardial sac by fibrous adhesions, after injection of the coronary arteries with a colloidal suspension of lamp black showed that the extracardiac anastomoses of the coronary arteries were increased owing to the presence of adhesions. In all four instances a particularly high injection of the parietal pericardium was obtained and microscopic examination of the adhesions showed them to contain injected vessels, extending from epicardium to parietal pericardium. A microscopical study of cleared blocks (3 mm. in thickness) of myocardium and attached pericardial adhesions, showed the arborization and anastomosis of branches of the arteries of the parietal pericardium with those of the heart. This vascularization was not limited to the usual areas of subepicardial fat but was seen in regions not ordinarily containing arterial branches. In no one of the four cases were the coronary arteries significantly diseased.

In one of the four cases, the normal sites of anastomoses between the cardiac and extracardiac vessels were destroyed by cutting away the great vessels entering and leaving the heart, as well as the peri- and intervascular reflections of parietal pericardium. Injection mass was found, however, in the arteries of the parietal pericardium and the diaphragm, showing that it has passed directly through the adhesions from coronary to extracardiac vessels.

If the extracardiac anastomoses of the coronary arteries constitute a significant reserve for cardiac circulation, it would appear that this reserve would be augmented by the presence of pericardial adhesions. Direct communication between branches of the coronary arteries and the pericardial branches of the internal mammary arteries with free anastomosis with the anterior branches of the thoracic aorta is established over areas corresponding to the extent of the adhesions. Work is in progress to study the functional significance of such an experimentally induced collateral circulation in experimental coronary occlusion.

Victor, Joseph: The Effects of Sugar and Electrolyte Solutions on the Metabolism and Irritability of Heart Muscle. Am. J. Phys. **103:** 620, 1933.

Isotonic solutions of potassium chloride and sucrose depress the oxygen consumption of irritable and nonirritable cardiac muscle. This is associated with a decrease

in muscle tone and loss of irritability. Isotonic calcium chloride increases both the tone and the metabolic rate of irritable and nonirritable heart muscle but renders the irritable muscle nonirritable. The antagonistic action of potassium chloride and sucrose and of calcium chloride on the metabolic rate and tone of heart muscle is found to be opposite that of irritable skeletal muscle. Furthermore, the action of these substances is independent of the previous state of irritability of heart muscle but varies with the previous state of irritability of skeletal muscle. If spontaneous sugar or potassium nonirritability in cardiac muscle is due to the same causes as obtain in skeletal muscle, the similarity of the action of sucrose and potassium solutions may be due to the washing away of calcium by the sucrose solution and thus increase the potassium chloride ratio at the surface membranes of the muscle fibers. Furthermore, if the differences observed are due to membrane equilibria, it might be suggested that heart muscle differed from skeletal muscle in having its membranes reversed and that a similar reversal of equilibrium was responsible for the phenomenon of nonirritability in skeletal muscle. Much more study, however, is required before theorizing in these matters will be profitable.

The metabolic rate of nonirritable cardiac muscle first decreases, then after several hours increases, and finally returns to normal after immersion in an isotonic solution of glucose. Ringer's solution slightly depresses the oxygen consumption of spontaneously nonirritable cardiac muscle but has no effect on the metabolic rate of irritable heart muscle.

Hydrochloric acid in concentrations above 0.01 M in isotonic sodium chloride decreases the oxygen consumption of spontaneously nonirritable heart muscle. Methylene blue increases the oxygen consumption of irritable and nonirritable heart muscle.

McGinty, Daniel A., and Miller, A. T., Jr.: Studies on the Coronary Circulation. II. The Absorption of Lactic Acid and Glucose and the Gaseous Exchange of Heart Muscle. Am. J. Phys. **103**: 712, 1933.

With the accumulation of data showing that lactic acid is absorbed by the heart of the dog in amounts corresponding to the quantity of material generally accepted as being oxidized as carbohydrate, it was found necessary to reopen the study of oxidations in cardiac muscle and to investigate the manner of disposal of absorbed lactic acid. Two methods were employed: first, perfusion of an isolated beating heart by arterial blood from a donor dog, and second, perfusion of the beating heart in situ. In either method, simultaneous samples of ingoing arterial blood and outcoming coronary venous blood were analyzed for lactic acid, glucose and oxygen and carbon dioxide content. Coronary volume flow of blood was recorded. Perfusions were carried out for thirty to ninety minute periods, blood samples being taken at five to nine minute intervals.

In 5 experiments on perfusion of the isolated heart with a total of 53 pairs of blood samples, the average lactic acid absorption was 1.5 mg., glucose absorption 0.2 mg. and oxygen absorption 3.5 c.c. per gram of heart muscle per hour. Blood flow amounted to 42 to 55 c.c. per gram per hour. In 7 experiments with the heart intact within the open thorax in 65 samples, average lactic acid absorption amounted to 3.1 mg., glucose 0.39 mg. and oxygen intake 5.1 c.c. per gram heart per hours. Mean coronary flow was 49 c.c. In the first group of observations, the respiratory quotient was below 0.70 in three and above 0.70 in two. In the latter group, a respiratory quotient below 0.70 occurred in but 1 experiment.

The results indicate that glucose is not absorbed at all or is absorbed in but small amounts while lactic acid is removed from the coronary arterial blood in quantities, which suggest its utilization as the carbohydrate fuel of the heart. The results of other workers who interpreted the loss of glucose from perfusion fluids as indicating

its absorption by the heart are criticized on the basis of failure to exclude decomposition of glucose as a result of bacterial action. This has been shown to be an important source of error in perfusion procedures. Furthermore, those who worked with blood as a nutrient fluid have failed to consider glycolysis in blood, which takes place with significant rapidity.

The status of the glycogen stores of the heart was not investigated; although a review of literature indicates that under the experimental conditions which prevailed, the glycogen content of the heart was neither increased nor drawn upon for carbohydrate oxidation. Significance of the respiratory quotient as an index to the fuel of the heart is criticized. It is believed that this quotient is of questionable value in determining the nature of oxidations in isolated organ perfusion. Under more normal experimental conditions, it may assume greater significance.

McCrea, F. D., and Wiggers, Carl J.: Rhythmic Arterial Expansion as a Factor in the Control of Heart Rate. Am. J. Phys. **103**: 417, 1933.

In a series of experiments, the heart rate changes which occur reflexly or directly when pulse pressure and mean pressure were varied as independently as possible were studied. Aortic pressures were optically recorded and systolic, diastolic and pulse pressures calculated from records by use of a calibration scale. Mean pressure values were arrived at accurately by measuring the area beneath the pressure curve and dividing by horizontal distance.

The effects produced by various procedures, such as compressing the vena cava and aorta, served no useful purpose in settling the problem, as pulse pressure and mean pressure changed in the same direction. They were useful in determining that under such conditions a mean pressure variation of 4 to 5 mm. is the minimal which causes any certain change in heart rate.

After saline infusion, which increases the pulse pressure, a cardiac slowing was obtained in a sufficient number of experiments in which no change or a decrease in mean pressure took place. These results were suggestive of a separate effect of pulse pressure but in view of some apparently negative effects could not be regarded as conclusive.

Through the expedient of producing experimental aortic insufficiency it was found possible to increase pulse pressure and simultaneously decrease mean pressure; further, by compressing the thoracic aorta to a suitable extent, mean pressure was often restored approximately or exactly to normal, while pulse pressures increased still more. It was found that frequently the heart rate slowed despite a sharp decline of mean pressure and with one exception was always retarded when mean pressure was restored to normal levels by compression. While the control of heart rate by pulse pressure changes was demonstrated, the results on the "whole animal" permitted no conclusions as to whether the effects were induced by direct or reflex action.

A second set of experiments was performed in order to determine whether changes of pulse pressures in a cephalic end of a perfused carotid artery can reflexly cause heart rate changes when mean pressure either remains unaltered or deviates in a reverse direction. To do this, pressure pulses were recorded simultaneously from the perfused carotid and the animal's own artery by means of optical manometers.

Perfusion of the cephalic end of a carotid artery with a constant pressure in the perfusion system was found not to produce a constant pressure within the artery itself owing to effects of collateral circulations. The magnitude of the pulsation varied inversely as the perfusion pressure used, being larger when pressures were low and small when they were high. Such dynamic effects complicate the interpretation of results of previous investigations.

A sudden change in pressure appeared more potent in producing temporary alterations in heart rate that permanent levels of pressure established. Alteration of the

perfusion pressures and rhythmical variations in such a way that pulse pressure increased in the perfused vessel while mean pressure remained unaltered or was even reduced were attended by cardiac slowing unless the reduction was too extreme. This demonstrates that pulse pressure variation dominates the production of reflex cardiac changes.

The conclusion is reached that Marey's law requires amendment; changes in mean pressure levels indeed control heart rate changes reflexly but only so long as pulse pressures do not change too much in an opposite direction. When this is the case, the effects of pulse pressure changes dominate the reactions.

Korns, Horace M., and Guinand, P. H.: Inequality of Blood Pressure in the Brachial Arteries, With Especial Reference to Disease of the Arch of the Aorta. J. Clin. Investigation **12**: 143, 1933.

The data obtained by bilateral brachial pressure measurements in 1000 normal subjects are presented and analyzed. What has been arbitrarily designated as a significant sphygmic inequality occurred 439 times in 378 persons; nearly three-fourths of the higher pressures were dextrolateral. Significant inequalities in pulse pressures appeared in 274 persons, 67 of whom failed to show differences of 10 mm. or more between the two systolic or diastolic levels; nearly three-fourths of the higher pulse pressures were dextrolateral. These pressures were measured simultaneously in both arms, but for all practical purposes consecutive measurement gives equally satisfactory results.

The fact that inequalities in the blood pressures and volume of the pulse in the right and left brachial arteries may or may not indicate disease of the aorta or its branches is illustrated by the presentation of case reports.

Sphygmic inequality without organic disease is probably always transitory, and it is reasonably certain that all normal persons manifest it at one time or another. The inequality may involve only the systolic pressures, or only the diastolic, or both; and if both levels are disparate, the inequality may be concordant (both right higher than both left, or vice versa) or discordant (right systolic higher than left and left diastolic higher than the right or vice versa). In some persons the higher pressure is irregularly heterolateral; in others it appears to be always homolateral. There is no evidence that right or left handedness plays any rôle. The physiology of transitory disparities in brachial pressures is not understood. Sphygmic inequality in the brachial or carotid arteries cannot be regarded as a sign of disease of the aorta or its branches unless it can be shown to be permanent.

Starr, Isaac, Jr., Collins, Leon H., Jr., and Wood, Francis Clark: Studies of the Basal Work and Output of the Heart in Clinical Conditions. J. Clin. Investigation **12**: 13, 1933.

Using a method devised by Starr and Gamble, involving a modification of the Henderson and Haggard ethyl iodide method for the estimation of cardiac output, the authors have made duplicate determinations of cardiac output and metabolism, repeated estimations of blood pressure and pulse rate and orthodiagrams in 50 individuals. These estimations were performed on fasting subjects lying at rest after a prolonged rest period. Those tested included apparently normal persons, persons who had recovered from congestive failure and patients with some circulatory abnormality but not immediately threatened with failure, namely, thyrotoxicosis, hypertension anemia, angina pectoris, compensated valvular disease, and functional heart disease. The authors present an extensive discussion of the details of the method together with a résumé of the technical difficulties encountered in carrying on such a study, particularly the estimation of the cardiac output and the establishment of basal conditions.

When the basal work of the left heart of these subjects was plotted against the volume of the heart or the area of the cardiac silhouette, the points representing cases

not threatened with failure were found to be arranged about a straight line. On the other hand, the points representing cases threatened with failure are outside the limits of the normal cases.

The results obtained are regarded as evidence that Starling's "Law of the Heart" holds for the basal cardiac work in diverse clinical conditions as well as for the heart lung preparation. Paraphrasing his words it may be said, "Within physiological limits the larger the size of the heart, the greater is the energy of its contraction." And as a corollary, when the work of any heart is not commensurate with its size, that heart is threatened with failure.

On the basis of a diverse group of cases believed to have normal myocardia, the authors have made a preliminary estimate of the normal relationship between heart work and size. Charts and equations are submitted by which the question of the normality of any case may be decided.

The relationship between heart size and heart work per beat was equally striking in 17 cases of hypertension. Those with hearts of normal size, by reducing cardiac output, maintained their hypertension without greater expenditure of cardiac work than normal persons. The patients with large hearts were performing increased work. Considering increased cardiac work as cause of hypertrophy in the latter group, its absence will explain the absence of hypertrophy in the former.

The cardiac output was directly related to the metabolism in the cases not threatened with failure. The arteriovenous oxygen difference was much smaller in these patients than in those who had been decompensated. The cardiac output was related to the size of the heart but, as a rule, not so closely as was the cardiac work. There was a surprising lack of correlation between cardiac output and body surface area in cases of hypertension; the remainder of the control cases showed correlation above the level of significance.

Although the errors in estimating basal cardiac output or work are undoubtedly large, the differences found in clinical conditions are so much larger that the results, properly interpreted, have clinical significance.

Levinson, Samuel A., and Learner, Aaron: Blood Cysts on the Heart Valves of Newborn Infants. Arch. Path. 14: 810, 1932.

In 16 consecutive postmortem examinations of infants, 12 showed blood cysts on the valves. These blood filled cysts appeared as small circumscribed, dark red, elevated nodules found on the mitral and tricuspid valve leaflets, infrequently on the pulmonic leaflets and rarely on the aortic. They varied in number from 2 or 3 to 10 or 15, though as many as 30 have been reported. The nodules project above the auriculoventricular leaflets near the free margin between the edge and the line of contact on closure. On histological examination, the nodules as seen in cross-section appear as monolocular or bilocular or even multilocular spaces filled with red blood cells. The spaces are lined by a single layer of endothelial cells, in appearance similar to the surface endothelium of the valve leaflets. A discussion is given of the possible manner of origin of these nodules.

Evans, William: Congenital Stenosis (Coarctation), Atresia, and Interruption of the Aortic Arch. Quarterly J. Med. 2: 1, 1933.

Instead of the usual classification proposed by Bonnett dividing cases of coarctation of the aorta into the infantile and adult types, the author proposes to introduce a classification whereby the cases are allotted to different groups according to the nature of the anatomical deformity present and the arrangement of the associated or compensatory lesions. In this way it would be possible to define six separate types of congenital stenosis and atresia of the aortic arch. In order to allocate a case to its particular group, it is necessary to consider the following data: (1) the site, nature and extent

of the constriction; (2) condition of the aorta proximal to the site of stenosis; (3) patency or otherwise of the ductus arteriosus; (4) relationship between the systemic and pulmonary circulation. The adoption of the proposed classification will also facilitate the interpretation of certain clinical findings presented by these cases and more especially will help to explain such appearances as are found on radiological examination of the heart and great vessels. It will also help to determine the nature of the changes that are the direct result of a modified circulation initiated by the presence of this congenital deformity.

The six types are enumerated as follows: Type I, congenital stenosis of the aortic arch with patent ductus arteriosus and hypoplasia of the proximal portion of the aorta. Type II, congenital stenosis of the aortic arch with a ductus arteriosus closed and hypertrophy of the proximal portion of the aorta. Type III, congenital atresia of the distal portion of the aortic arch with ductus arteriosus closed and hypertrophy of the proximal portion of the aorta. Type IV, interruption of the aortic arch in its distal portion with a ductus arteriosus widely patent and hypoplasia of the proximal portion of the aorta. Type V, congenital atresia of the proximal portion of the aortic arch with a ductus arteriosus patent. Type VI, congenital absence of the ascending aorta with patent ductus arteriosus. Features that characterize each of the six types are outlined, and a short description of the cases is appended in each group.

In a study made on 28 cases of congenital stenosis, atresia or interruption of the aortic arch, 26 of which had been examined at autopsy, it was found possible to separate the cases into definite types according to the anatomical features present.

Patients living beyond early infancy were found in Types I, II and III only; few in Type I with the ductus patent and more in Types II and III with the ductus closed. Other developmental abnormalities that may accompany this congenital deformity of the aortic arch are enumerated.

No one symptom or collection of symptoms could be claimed to indicate with certainty the diagnosis of congenital stenosis of the aortic arch. In infants the exact nature of the lesion can only rarely be established. A tentative clinical diagnosis of congenital heart disease is usually made. It is also rare for any subjective symptom occurring in an adult suffering from this condition to direct attention to the initial lesion which has caused the illness. The author believes that symptoms presented by one of the patients may prove peculiar to, or either pathognomic of, the condition. This patient complained of numbness and weakness in both legs whenever he assumed the upright posture after reclining for some little time in the horizontal position. As he changed from the latter to the former posture, he experienced a sensation of "blood rushing back to the legs." He states that the sensation was comparable to the one he experienced when the pressure within the pneumatic bag of the sphygmomanometer placed around the thigh was released. These symptoms disappeared on walking a short distance and were never precipitated by the act of continued walking. It is seldom very safe to rely upon physical signs obtained from examination of the heart as indicating the diagnosis of this congenital lesion. The deformity is a vascular one, but owing to its proximity to the heart, the latter does undergo certain changes which have been described and which give rise to certain physical signs. A short note has been added on the prognosis and manner of death in patients presenting this congenital anomaly.

Graef, Irving, Parent, Solomon, Zitron, William, and Wyckoff, John: Studies in Rheumatic Fever. I. The Natural Course of Acute Manifestations of Rheumatic Fever Uninfluenced by "Specific" Therapy. Am. J. M. Sc. **185**: 197, 1933.

This study is based on a series of 162 patients suffering from acute rheumatic fever admitted to the hospital during two years. The observations made on 105 of these patients receiving no form of therapy which might be considered specific and no antipyretic drug formed the basis of the report. Only 47 of the 105 patients fulfilled the

criteria set up for purposes of the study. It is concluded that in adolescence and adult life the acute manifestations of rheumatic fever tend to subside spontaneously. These manifestations vary in number, degree and duration, and are discussed by the authors.

If changes in the number, degree and duration of manifestations are used as criteria for determining the effect of therapeutic agents, such changes must be compared either with a standard control group of rheumatic fever patients of known age, sex, racial and proper geographical distribution, of sufficient size to meet statistical requirements; or controlled cases must be studied simultaneously with cases receiving "specific" therapy, in sufficient number so that it may be determined whether or not the effects associated with treatment are not simply variations attendant on the natural course of the disease.

Clawson, B. J., Wetherby, Macnider, Hilbert, E. H., and Hilleboe, H. E.: Streptococcic Agglutination in Chronic Arthritis and Acute Rheumatic Fever. Am. J. M. Sc. **184**: 758, 1932.

Streptococcic agglutination titers were determined in chronic arthritic and acute rheumatic fever patients for two strains of streptococci. The first strain was isolated from a case of acute rheumatic fever and the second from a case of chronic arthritis. Comparing the agglutination titers of the above conditions with those of normal persons and of patients with scarlet fever and glomerulonephritis, with the rheumatic strain the agglutination titers of acute rheumatic patients were higher than normal, while those of the chronic arthritic patients were not. With the chronic arthritic strain, the titers were higher than normal in both chronic arthritis and acute rheumatic fever, but higher in the latter. With both strains the titers were decidedly higher than normal in both scarlet fever and glomerulonephritis. In all tests including the normal serums, the chronic arthritic strain was agglutinated in higher dilutions than the acute rheumatic strain. The chronic arthritic strain appeared to be more sensitive to agglutination.

These findings suggest that both chronic arthritis and acute rheumatic fever are streptococcic infections. The view that chronic arthritis is due to a specific strain is not supported, since the chronic arthritic strain was agglutinated in higher dilutions with serums from acute rheumatic fever patients than with the serums of patients with chronic arthritis. The lack of strain specificity is also shown by the fact that both the rheumatic and the arthritic strains were agglutinated in higher dilutions with serums from scarlet fever and glomerulonephritis than with the serums from acute rheumatic fever or chronic arthritis.

Collis, W. R. F., Sheldon, Wilfrid, and Hill, N. Gray: Cutaneous Reactions in Acute Rheumatism. Quarterly J. Med. **1**: 511, 1932.

The present investigation was undertaken with the view to elaborating and confirming previous observations with hemolytic streptococcal endotoxin on a larger series of cases and at the same time ascertaining whether any analogy existed between the cutaneous reactions to this hemolytic streptococcal extract and to similar products of nonhemolytic streptococci and other pathogenic bacteria.

Skin reactions of 303 rheumatic children have been tested, while 256 nonrheumatic children have been similarly examined to serve as controls. The rheumatic series consisted of children who were at the time suffering from or had previously suffered from polyarthritis, carditis or chorea.

The results obtained indicate that rheumatic children are more sensitive to streptococcal extract than are nonrheumatic children, and that of the rheumatic children those with chorea are the most sensitive. Children with active rheumatism, and for a period of six months after the acute attack, show a high percentage of strongly positive reactions (80 per cent). After six months, this reactivity diminishes. Children with ful-

minating carditis lose their skin reactivity during the severe phase of their illness, though they tend to regain it later. Patients with chronic cardiac failure also tend to give much reduced reactions. Age seems to be an important factor in determining the probability of positive reactions up to the age of puberty. The curve is seen to rise in an almost straight line up to twelve to fourteen years, after which it ceases to rise.

Skin reactions to hemolytic streptococcal extracts appear to bear no relation to skin reactions with hemolytic streptococcal exotoxin (Dick toxin).

A comparative study of the skin reactions of extracts of hemolytic, green and non-methemoglobin forming streptococci appears to indicate that these extracts do not contain a common active principle but that each extract gives a specific skin reaction. Rheumatic children, when tested to extracts of two viridans streptococci and one gamma streptococcus, only showed a higher percentage of strongly positive reactions to one of the viridans extracts than did the controls.

Skin reactions of rheumatic children to tuberculin, Schick toxin and extracts from pneumococci, staphylococci, diphtheroid bacilli and Pfeiffer's bacillus do not show a higher sensitivity than do nonrheumatic children and thereby differ from the skin reactions produced by hemolytic streptococcal extract.

Book Reviews

L'Angine de Poitrine: Formes Cliniques, Traitement Médical et Chirurgical. By Camille Lian with the collaboration of A. Blondel, G. Huret, M. Marchal and H. Welti, 429 pages, Paris, Masson et Cie, 1932.

The authors divide *angor* into five types: (1) cardio-arterial, (2) cardiac, (3) reflex, (4) toxic, and (5) neurotic. The cardio-arterial type which includes four-fifths of all cases has three subdivisions: (a) the common form of cardio-arterial angor, (b) acute febrile coronary angor, and (c) abdominal angor. The cardio-arterial angor is regarded as due to overburdening of the left ventricle whether from vasomotor disturbance, coronary stenosis, aortitis or "hypertrophic dilatation." The so-called cardiac angor is caused by such conditions as rheumatic valvular disease or paroxysmal tachycardia. Reflex angor is due to gastrointestinal disturbances, cholelithiasis or left-sided thoracobrachial neuralgia. It occurs in the absence of heart disease. Toxic angor is due to intoxication from hypothyroidism, gout, or tobacco, although the last is seldom important. The neurotic type is an hysterical pseudo-anginal phenomenon.

Most of the book is devoted to clinical descriptions of the various types of angor. A few pages are given to the pathological anatomy of acute febrile coronary angor. The electrocardiographic findings of the common form and the acute febrile coronary forms of cardioarterial angor are discussed.

Considerable space has been devoted to treatment. The three "treatments of choice" in the so-called cardio-arterial angor are: (1) intravenous injection of iodides, (2) subcutaneous injection of carbon dioxide, and (3) irradiation. Most of the other methods of treatment, including a variety of drugs, hygienic, physiotherapeutic and surgical procedures are mentioned. Removal of the stellate ganglion is discussed in some detail, although only two of the authors' cases were subjected to this procedure.

The references, which are mainly to the French literature, include 37 papers by the senior author. The book will therefore be of interest to all who wish to acquaint themselves with contemporary French thought on the subject. The reader, however, will not find an authoritative discussion of the recent work on the relationships between disturbances in blood supply of the myocardium and anginal types of pain. Recognition of the importance of this work should have compelled a new classification and a rewriting of the sections dealing with the causes of anginal types of pain. These defects seriously limit the usefulness of the book. —*C. C. W.*

The Heart Rate. By Ernest P. Boas and Ernst F. Goldschmidt. 1932, 166 pages, Springfield, Ill., and Baltimore, Md., C. C. Thomas.

Boas and Goldschmidt present in a small volume the results of an extensive study of the heart rate in 356 individuals, 103 of them being normal controls. They employed the Boas cardiotachometer, an electrical instrument which amplifies and records the action current of each heart beat. The machine is attached to the subject of the experiment by means of long leads so that it is possible to observe all sorts of bodily activity during the day and what is just as important, the phenomena of sleep. The authors have investigated the many factors which influence heart rate, especially the results of emotion, exercise, hot and cold food and the varying conditions of sleep. Particularly instructive are their observations on the morning toilet which in several normal controls raised the pulse rate above 110. The many excellent tracings in the book record the effects of those homely and intimate events of daily life which have escaped scientific

study in normal people, although it is well known that they may precipitate acute cardiac failure in patients with heart disease.

Perhaps the most illuminating data for clinicians are the averages obtained on the 51 normal men and 52 normal women, most of whom were young:

	AV. RATE FOR WAKING HOURS	BASAL AWAKE	AV. RATE FOR SLEEPING HOURS	MINIMUM ASLEEP
Men	77.8	61.4	59.4	52.8
Women	83.9	69.9	65.3	57.7

The authors emphasize the importance of obtaining true basal conditions for comparative purposes, and they point out the clinical value of measurements made during sleep, especially in the differential diagnosis of neurocirculatory asthenia. Their detailed studies of the heart rate in cardiac patients are of great interest. The curves of rates during the different stages of operations should be scrutinized by internists as well as surgeons.

This little book is one that should not be neglected by physicians or physiologists. The subject matter is well presented and the authors keep a good sense of proportion. They do not lose sight of the fact that the heart rate is only one of many factors in the circulation. —*E. F. Du B.*

THE FAILING HEART OF MIDDLE LIFE. By A. S. Hyman and A. E. Parsonnet. The F. A. Davis Co., Philadelphia, 1932.

This book, with greater accuracy, might have been entitled "coronary arterial disease," inasmuch as five-sixths of the text is devoted to this subject. Of the heart that fails in middle life as a result of rheumatic, syphilitic, or hypertensive disease, nothing is said.

It is not made clear for whom the book was written. There are intimations that it is intended for the practitioner, but if so, it is scarcely justifiable to devote almost a fourth of its pages to a detailed discussion of electrocardiograms, and another fourth to an exhaustive presentation of the various theories relating to angina pectoris. The general approach of the authors is revealed in their statement: "Indeed, the very approach to the simplest discussion of the anginal syndrome must carry one over pathways of the most intangible and complicated sort, proceeding through a labyrinthine maze of neurologic, myogenic, and teleologic routes." In view of this attitude, with which the present reviewer is not in sympathy, it is not surprising that the chapter on angina is the longest and most involved in the volume. It is regrettable that their learned discussion of this type of heart failure should leave the careful reader with his impressions blurred and confused rather than clarified, for there are many features of angina that may be described clearly and dogmatically, even though some are still puzzling.

The book as a whole leaves the impression of being too long; with the exception of the last chapter, it would have been improved by considerable reduction. In their apparent desire to leave no topic untouched, the authors have extended their discussions and descriptions unduly, and in many instances have introduced confusion rather than clarity. It is by no means clear to the present reviewer, even after several readings, just what is their conception of myocardosis. They speak of it as "a designation spelling a new approach to the understanding of the earliest manifestations of coronary and myocardial insufficiency," and in many places indicate that the term applies to early changes in the heart. Yet throughout their discussion they speak of early myocardosis, and never of later or advanced myocardosis. The pain of this condition is discussed at

length, but nowhere is it made clear how it differs from that of true anginal failure. One can scarcely believe that they have justified the use of this newer term as a substitute for arteriosclerotic heart disease; with their declaration that the term "myocarditis" is no longer tenable there can be no serious quarrel.

The book is written interestingly and in many places eloquently, with a happy choice of words and descriptive phrases, but without sufficient thought of conciseness. The illustrations are uniformly excellent. The last section, devoted to the medicolegal aspects of sudden death from heart disease, is a most valuable addition to a modern text in this particular field. There is a very complete bibliography containing 1250 references, and a complete index. To me it seems a stimulating, thoughtful, and comprehensive presentation of an increasingly important subject, but one which will be of chief value to the cardiologist or the practitioner who has a special interest in diseases of the heart. *H. M. M.*

DIE SOZIALE BEDEUTUNG UND BEURTEILUNG DER KREISLAUFERKRANKUNGEN. By Dr. med. Franz Grünbaum. Georg Thieme, Leipzig, 1933, pp. 128. (Arbeit und Gesundheit. Herausgegeben von Prof. Dr. Martineck. Heft 21.)

This small monograph deserves especial notice in the United States, for, as is manifest, it owes its inspiration to phases of interest in the heart diseases which have been cultivated especially in this country. Doctor Grünbaum has, as a matter of fact, travelled about here to be acquainted with the current course of events. The fact that his book is published in the series "Arbeit und Gesundheit" is evidence of the growing concern in Germany with aspects of the heart diseases from the point of view of the public health. It is, furthermore, not without interest to record the occurrence of the first meeting in Germany of the "Wissenschaftliche Komitee zur Erforschung und Bekaempfung der Kreislaufstoerungen" in March, 1933. Leadership in interest in this problem is a development in which we may take a legitimate pride.

The specific matters which have occupied Doctor Grünbaum are statistics of mortality and morbidity in relation to age. He made comparisons between experience in the United States and in Germany and studied the relation of etiological moments to the frequency of the various groups. In arriving at diagnoses, use has been made of the classification of the New York Heart Committee. In their study of functional classification Grünbaum mentions the effort of Fraenkel and Doll who have attempted a separation based on the reactivity of patients to the intravenous injection of strophanthin. This is a method which requires further consideration but one which surely is liable to serious error. Other criteria are discussed dealing with physical examination and with efficiency—in valvular diseases and in arrhythmias.

The points of view which have received so much attention here in recent years have clearly awakened a response abroad. The importance of this newer plan of understanding the course of events of a disease as it concerns both individuals and communities will become more apparent when, as the result of sifting ideas in various countries, the effort is finally made to devise a working nomenclature of morbidity. In the development of any science, nomenclature or language is obviously fundamental. That this is being found to be the case in connection with the study of diseases is not unexpected when experience in other sciences, physical and biological, is recalled. *A. E. C.*

NOUVEAU TRAITÉ DE MÉDECINE. FASCICULE X, PATHOLOGIE DE L'APPAREIL CIRCULATOIRE (COEUR ET VAISSEAUX). Vol. I 992 pp., and Vol. II 778 pp., Masson & Cie, Paris, 1933.

This monumental work, planned by Professor Teissier but completed under the direction of Professor Lutembacher, is a compilation of most of the facts and many of the theories pertaining to the circulation. Its high quality may be judged from the names of the contributors—Lutembacher, Teissier, Prieur, Bordet, Giraud, Coste, Dumas,

Duvoir, Mouquin, Durand, Lian, Rouvière, Pichon, Béthoux and Devé. Volume I contains sections on anatomy and physiology; on the various syndromes, the arrhythmias, angina pectoris and heart failure; and on treatment and the pharmacodynamics of a large number of drugs. Volume II includes discussions of the usual and unusual diseases of the heart—pericarditis, endocarditis, myocarditis, coronary disease, congenital defects, injuries, syphilis, tuberculosis, actinomycosis, echinococcus cysts and tumors. Volume III, the section on diseases of the vessels, is still to appear.

The work is inclusive rather than selective. Each chapter is written by a man well qualified in his field, and each chapter is interesting, but on going over the work as a whole one feels that it has been impossible to avoid repetition or to preserve that balance in the discussion which will give the reader a clear sense of the distinction between the essential and the nonessential. Throughout the text there are frequent references to the literature, particularly to the French literature, but unfortunately the curious reader who wishes to look up these references will find no adequate bibliography to help him. An alphabetical index, in addition to the detailed table of contents, would add to the value of the book. *E. H.*

Syphilis des Herzens und der Gefässe. (Vol. 16 of Medizinische Praxis, Sammlung für ärztliche Fortbildung. Herausgegeben von L. R. Grote, A. Fromme, K. Warnekros.) By Prof. Dr. Ed. Stadler, Leitender Arzt der Inneren Abteilung des Stadtkrankenhauses Plauen i. V. Pp. 82 with 8 illustrations. Dresden and Leipzig, Theodor Steinkopff, 1932.

This brochure of eighty pages is one of a series of small volumes on medical practice intended for general practitioners. In it the experienced author presents a compact and well-balanced picture of the various aspects of syphilis of the heart and arteries. The arrangement of the book is orderly, and the pathological and clinical descriptions are concise and clear. The usefulness of the volume is increased by the comprehensive summaries placed at the end of each section and by a few well-chosen illustrations.

The greater part of the book is, very properly, devoted to syphilis of the aorta, and this subject is treated with admirable clarity and thoroughness. Much attention is given to a consideration of the treatment of luetic aortitis, with insistence upon the necessity of prolonged, thorough antiluetic therapy, including the arsenicals, even in cases complicated by aortic insufficiency and by anginal pain. Emphasis upon the need of caution and judgment in the use of the arsphenamines, however, is not lacking.

No attempt is made to furnish a complete bibliography, but a list, predominantly German, of the more important recent writings upon the subject of cardiovascular syphilis is appended.

As an epitome of our present knowledge of this vastly important subject the volume merits cordial commendation. *L. A. C.*

Resultats du Traitement Chirurgical de l'Angina de Poitrine Récueil de 54 Observations de Methode de la Suppression du Reflexe Presseur et de 82 Observations de Sympathectomie Avec Ganglion Étiole. Par D. Danielopolu. Pp. 285, with 8 figures. Bucarest, Impr. Cultura, 1932.

The monograph is based upon a careful analysis of the surgical treatment of the cases of angina pectoris; 52 according to the Danielopolu method (suppression of the pressor reflex) and 82 with removal of the stellate ganglion, according to the method of Franck-Ionnesco-Gomoiu.

Danielopolu calls his method that of the suppression of the pressor reflexes. He advises the resection of the cervical sympathetic chain, without removal of the stellate ganglion but with section of the fibers of the cervical vagus which enter the thorax, and sections of the vertebral nerves, and of the communicating branches which unite the inferior cervical ganglion and the first thoracic to the sixth, seventh, and eighth cervicals

and the first dorsal roots. Operation is first performed on the left side and then if necessary, on the right. Even if the radiation of pain is to the right side, the operation is performed on the left side as the left ventricle is assumed to be the site of origin of the pain. Ether is the anesthetic of choice. Of the 54 cases operated upon according to the principle of Danielopolu, 70 per cent were greatly relieved or cured for a period of from three months to one year, while only 51 per cent, in 82 cases in which the stellate ganglion had been removed, were relieved or cured. There were 22 per cent of failures with the author's method and 33 per cent with that of Franck-Ionnesco-Gomoiu. The operative mortality was very much lower in the former, being 1.8 per cent, and in the latter 17 per cent.

The value of any therapeutic procedure depends upon the accuracy of the anatomical diagnosis. The reviewer is unable to determine the type of case for which the author advocates surgical interference.

Anatomically the author classifies as centripetal cardio-aortic nerve trunks; the centripetal fibers passing through the stellate ganglion to the second, third, and fourth dorsal vertebral roots, the vertebral nerve, the cervical sympathetic, and the pressor and depressor fibers of the vagus passing to the inferior cervical ganglion. He maintains that the centripetal fibers passing to the second, third, and fourth dorsal roots are pressor, and excitation of the medullary end causes a rise in blood pressure in the majority of cases. The vertebral nerve, on excitation, based upon experiments in 8 dogs and 3 cats, gives pressor effects. The cervical sympathetic chain has both pressor and depressor effects. The branches from the vagus nerve have also pressor and depressor effects.

The pressor phenomena are defined as an exaggeration of the predominant factors of the cardiovascular mechanism: automatism, excitability, conductivity, and cardiac and vascular contractility. Depressor phenomena are defined as a diminution of any or all of these properties.

The centripetal fibers, through their connections with the cerebrospinal system, convey sensitivity and thus the sensation of pain is felt. The hypothesis assumes that the toxic products of fatigue accumulate in the myocardium due to a disproportion between the work done and the coronary flow. A pressor reflex results and this pressor reflex increases the burden of work on the heart. This increases the intoxication which results in motor and sensory phenomena which we call angina. The author then states: "To prevent angina we must cut the centripetal paths of the pressor reflex." The author definitely states that the sympathetic fibers passing through the stellate ganglion to the coronary vessels are vasodilatory and that the parasympathetic fibers passing through the vagus are vasoconstrictors. If one accepts this statement, then the removal of the stellate ganglion destroys the nerve trunks which cause dilatation of the coronary vessels. This is the author's thesis, and is his main argument against the operation of Franck-Ionnesco-Gomoiu, and also against the school of Leriche and Fontaine. Page after page reiterates this and each individual case is analyzed on this basis. The cause of immediate and remote death following the operation is believed to be due to this fact. The author further states that the destruction of the vasodilatory fibers increases the "myocarditis" of angina. It is somewhat difficult to see how this quite fits the theory or to know what the author means by "myocarditis" of angina.

The anatomical researches of Ranier and H. Dumitresco are important. They made careful dissections of the sympathetic nervous system on twelve cadavers and twenty-five fetuses. Their general conclusions are as follows: The stellate ganglion is composed of three parts: intermediary, cervical, inferior, and first thoracic. It can be either a single mass caused by the fusion of the three, or in two parts: an antero-internal situated before the vertebral artery which is the internal ganglion, and the posterio-external formed from the cervical inferior and the first thoracic, or it may consist of two ganglionic masses formed by the fusion of the intermediary ganglion to the inferior cervical and by the first thoracic alone.

The intermediary ganglion gives off the important cardiac inferior nerves. Extirpation of this ganglion is a partial stellectomy. The cervical inferior ganglion gives off several cardiac inferior nerves, more than that of the first thoracic. Extirpation of this ganglion is therefore a partial stellectomy. The middle cervical ganglion may be lower and be in two parts and may be mistaken for the intermediary ganglion. The vertebral nerve practically always arises from the superior pole of the inferior cervical ganglion. Therefore extirpation of this ganglion must destroy the vertebral nerve.

This monograph is a contribution to the study of the physiology of the sympathetic nervous system and of the innervation of the heart. The dissection of the anatomists and the illustrative drawings of the sympathetic and parasympathetic nervous system with their connections to the central nervous system are rather schematic, and if subsequent work substantiates the anatomical facts, further physiological experiments are needed to prove the many contentions of the author.

The value of the surgical treatment of the pain syndrome of angina is still uncertain. In general there is less enthusiasm for the operative treatment of angina pectoris than at the time the method was originally proposed. The author does not comment on the method of paravertebral block anesthesia as originally proposed by Swetlow. This method appears to be safer and is at least associated with practically no mortality. The surgery of the sympathetic nervous system is still in its early stages, and the reviewer feels that much more must be learned before one can be partisan in the many controversial matters concerning the anatomy, physiology, and pharmacology of the vegetative nervous system. *M. A. R.*